“CLINICO HISTOPATHOLOGICAL CORRELATION IN VARIOUS SPECTRUM OF LEPROSY”

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(BRANCH XX)

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CERTIFICATE

Certified that this dissertation titled "**CLINICO HISTOPATHOLOGICAL CORRELATION IN VARIOUS SPECTRUM OF LEPROSY"** is a bonafide work done by **Dr. B. AMALA,** Post-graduate student of the Department of Dermatology, Venereology and Leprosy, Madras Medical College, Chennai – 3, during the academic year 2012 – 2015. This work has not previously formed the basis for the award of any degree.

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I, **Dr. B. AMALA** solemnly declare that this dissertation titled "**CLINICO HISTOPATHOLOGICAL CORRELATION IN VARIOUS SPECTRUM OF LEPROSY**" is a bonafide work done by me at Madras Medical College during 2012-2015 under the guidance and supervision of **Prof. K.MANOHARAN, M.D., D.D.,** Professor and head department of Dermatology, Madras Medical College, Chennai-600003.

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CONTENTS

ABSTRACT

Introduction: Leprosy is a chronic, infectious disease caused by Mycobacterium leprae. It is classified into five groups based on clinical, histological, microbiological and immunological criteria (Ridley & Jopling Classification). However, a great variation has been observed in the interpretation of histopathological examination of skin biopsies and clinical presentation of the disease. Histopathological examination of skin provides confirmatory diagnosis in suspected cases and gives indication of progression and regression of disease under treatment. This study is intended to demonstrate the concordance between clinical and histopathological diagnosis in leprosy.

Method: : All cases attending the Hansen OPD were examined clinically and Slit Skin Smear was taken and stained with Ziehl-Neelsen stain for Acid Fast Bacilli. Skin Biopsy specimen was obtained from clinically diagnosed cases of Leprosy and stained with Hematoxylin & Eosin and modified Fite Ferraco . The clinical diagnosis correlated with histopathology in all 50 cases.

Result: The age of the patients was ranged from 7 to 65 years. The male to female ratio of patients was 4.5 to 1. The majority of cases were in the age group of 21-40 years belonging to low socioeconomic status. Borderline tuberculoid was the most common presentation. Highest parity was observed in LL(92.9%). Clinco-histopathological agreement was seen in 40 (80%) cases, 10 (20%) cases shows disagreement.

Conclusion: The clinical and histopathological features along with bacteriological index are useful than any single parameter in arriving definitive diagnosis and classification of the leprosy.

INTRODUCTION

Leprosy, also known as Hansen's disease, is one of the oldest disease of mankind. Leprosy still remains an important public health problem in many parts of Asia, mainly in India.

In our country despite declaring leprosy elimination at national level in January 2006 it is still a disease of endemic in many states. The total estimated global new cases detected in 2009 were 2, 27, 849 and India account 1,33,717 (58.7%) cases.

Depending on the immune status of the host, Leprosy presents in various clinico-pathological forms. Leprosy can be diagnosed by various methods including detailed clinical examination of the skin lesions and peripheral nerves, demonstration of the Acid Fast Bacilli (AFB) in slit skin smears by Ziehl-Nielsen staining, Histopathological section, demonstration of bacilli by modified Fite Faraco procedure[10], and Fine Needle Aspiration Cytology (FNAC) of nerves.

Ridley and Jopling have suggested immunological basis of leprosy and classified into five types as Tuberculoid Leprosy (TT), Borderline tuberculoid Leprosy (BT), Mid-borderline Leprosy (BB),

Borderline Lepromatous Leorosy (BL), and Lepromatous Leprosy (LL). This Classification is accepted worldwide and is highly recommended.

Though the clinical diagnosis is based on characteristic hypopigmented patches with sensory loss, a great variations are seen in interpretation of these Hypopigmented skin lesions both clinically and histo-pathologically.

So along with provided detailed clinical information and bacilloscopic examination, skin biopsy play an important role in the diagnosis of leprosy. Histopathological Examination also helps us to ascertain the immunological status of the individual by which we can predict the response to the treatment.

This research is taken to study the correlations between the clinical and histo-pathological diagnosis of leprosy patients, and to evaluate the importance of skin biopsy for the diagnosis of leprosy.

REVIEW OF LITERATURE

DEFINITION

Leprosy is a slowly progressive, chronic granulomatous, infectious disease caused by Mycobacterium leprae, and affecting the skin, peripheral nervous system and certain other tissues.

HISTORICAL ASPECTS OF LEPROSY

Leprosy is a very ancient disease. The earliest possible account of a disease that many scholars believe is leprosy appears in an Egyptian Papyrus document written around 1550 B.C. Around 600 B.C. Indian writings describe a disease that resembles leprosy. It has also found mention in vedic writings as Kusht around 1400 BC. [1]

The disease was probably carried from India to Europe in the 4th century BC by returning soldiers and camp followers from the Greek wars of conquest in Asia, led by Alexander the Great. However the earliest description of the disease as elephantiasis was unmistakably leprosy by Arateus, in Greece, about 150 AD. [2]

Through ages, leprosy has been feared and misunderstood, and has resulted in significant stigma and isolation of those who are afflicted. It was thought to be a hereditary disease, a curse and a

punishment from the Gods. During the Middle Ages, those with leprosy were forced to wear special clothing and ring bells to warn others of their coming. [3]

Noble families founded Leprosoria, hospitals for leprosy patients between 12th and 15th centuries. Leprosy patients were legally considered dead during that period.[4]

Moller Christensen's work revealed that 80% of the skeleton excavated at Naestved, Denmark showed the pathognomonic bony changes.[5]

Carl William Boeck (1808 – 75) and Daniel Cornelius Danielssen (1818 – 94), from Norway, two renowned leprosy experts of the nineteenth century, believed that leprosy was a congenital disease and not an infectious one.[6]

Dr. Gerhard Henrik Armauer Hansen (1841-1912) Danielssen's son-in-law, was the first person to identify the germ that causes leprosy under a microscope (1873). Hansen's discovery of Mycobacterium leprae proved that leprosy was caused by a germ and was thus not hereditary, from a curse, or from a sin.[7]

In 1882 Paul Ehrlich described the property of acid fastness.[8] Schaffer in 1898 made a study in spread of leprosy by aerosols.[9]In 1909 Paul Unna postulated clustering of the bacilli into “globi” and showed the cell free sub epidermal zone in histological sections.[10]

In 1921, U.S. Public Health Service established the Gillis W. Long Hansen’s Disease Center in Carville, Louisiana, which came to be known as “Carville.” It became a center of research and testing to find a cure for leprosy and a live-in treatment center for leprosy patients.

EPIDEMIOLOGY

GEOGRAPHICAL DISTRIBUTION

Although the worldwide prevalence of leprosy is less than one per 1000, still it is a public health problem in 15 countries including India, Brazil, Myanmar and Nepal.[11]

The prevalence rate of leprosy in 2012 was 181 941 (0.34), compared to 189 018 (0.33) at the end of the first quarter of 2013. The overall incidence of new cases in 2012 was 232857, relatively greater figures compared to earlier years. The South-East Asia Region accounted for 71% of new cases detected worldwide, with 16% from

Americas, 9% from the Africa Region and 2% each from the Eastern Mediterranean and Western Pacific Regions.[12]

India contributes 58% to the world leprosy burden. In 2012-13, India recorded 83,000 leprosy cases with a prevalence of 0.68 per 10,000 population. 33 states had attained the elimination level of less than one case per 10,000 population. Two States, Bihar and Chattisgharh are yet to achieve elimination (with a prevalence rate of 1.12 and 1.94, respectively). Of the total of 640 districts, 110 districts still have prevalence rates between 1 and 2/10000, while in 530 districts, elimination has been achieved.[13]

FACTORS IN TRANSMISSION OF LEPROSY

1.Agent factor

2.Host factors

3.Environmental factors

4.Social factors

1. AGENT FACTORS

Leprosy is caused by Mycobacterium leprae. These are obligate intra cellular parasite. M.leprae is a straight or slightly curved slender,

capsulated, non-motile, non spore forming, acid- fast staining rods which can be seen as clumps or bundles on microscopic examination. They divides into two in every 12 to 14 days. These are non cultivable in artificial culture medium.[14]

M.leprae grows in cooler tissues like skin, peripheral nerves, upper respiratory tract and testis, sparing warmer areas.[15]

The ultrastructure of M. leprae:

- Capsule
- Cell wall
- Cell membrane
- Cytoplasm

CAPSULE

Capsule is composed of phthiocerol demycocerosate and phenolic glycolipid-1. This lipid capsule protects the bacteria from lysosomal enzymes.PGL-1 is highly immunogenic, generating IgM class of antibodies, demonstrable in 60 % of TT and 90 % of LL patients.[16,17]

CELL WALL

This outer coat of bacteria protects from environment and gives definite shape to the bacterial cell. It has an inner electron dense and an outer electron transparent layer. It is composed of peptidoglycan-arabinogalactone- mycolic acid complex, alternating N-acetylglucosamine and N-glycolylmuramate linked by peptide cross bridges, which are linked to the galactan layer by arabinogalactan. Mycolic acids are linked to the terminals of arabinan chains to form the inner leaflet of a pseudolipid bilayer. The outer leaflet is composed of an array of intercalating mycolic acids of trehalose monomycolates and mycoserosolic acids of phthiocerol dimycocerosates as well as phenolic glycolipids. Cell wall is the last structure to disappear with chemotherapy.[18,19]

CELL MEMBRANE

It contains proteins which controls the active and passive transport of substances across inside and outside of the cell. Two major proteins are extracted, which are major membrane protein-I(MMP-I) and major membrane protein-II(MMPII).[20] MMP-I is a 35kDa protein. The MMP-II is identical to mycobacterial bacterioferritin and it has

large molecular mass of 380kDa.[21] Cell membrane also contains phospholipids.[22]

CYTOPLASM

M.leprae cytoplasm contains three major proteins with molecular weight of 28 kDa, 17 kDa and 28 kDa.[20] It also contains storage granules, DNA and RNA.

M.leprae can survive outside the human body for 2 to 9 days.It secretes certain enzymes like superoxide dismutase and catalase, also has DOPA oxidase activity.[15, 16]

2. HOST FACTORS

Age:

Leprosy is more commonly seen in the age group 20 – 30 years, but can occur at all ages from infants to very old age. In endemic areas, it can occur in children, which indicates presence of active transmission of the disease in the community.[23]

Sex:

Leprosy in adults is more prevalent among males than females, genarally in the proportion of 2:1. In children there is no significant difference between sexes.[23,24]

Migration

Due to migration of population from rural to urban areas, leprosy cases have increased in urban areas in recent years.[15]

Immunity

Occurrence of the disease depends on immunological status of an individuals. Cell mediated immunity is most important resistance against M.leprae, which is evidenced by development of protection against leprosy after BCG vaccination.[15]

Genetic factors

Many studies suggest that, among monozygotic twins if one had leprosy, the other almost always had leprosy, but this was not seen in dizygotic twins.[25]

HLA association

- Tuberculoid Leprosy DR3
- Lepromatous Leprosy DQ1[26]

Familial Clustering

The occurrence of Leprosy is more in family clusters. The risk of a person developing leprosy is 4 times higher when the leprosy contacts

are in neighbourhood; the risk is increased to 9 times if the contact is within immediate household and even higher if they are multibacillary.[27, 28]

3. ENVIRONMENTAL FACTORS

The risk of transmission is more in humid conditions, because humidity favours the survival of M.leprae.The bacilli remain viable in moist soil at room temperature for 46days.[29]

4. SOCIAL FACTORS[30]

- Overcrowding
- Lack of education
- Poor personal hygiene
- Lack of ventilation

TRANSMISSION FACTORS

Source of infection: [31]

The only source of infection is a leprosy patient. All patients but only those capable of discharging bacilli from their body are known as infectious or open cases belonging to lepromatous pole. On the other

hand, patients unable to shed bacilli are known as non-infectious or closed cases belonging to tuberculoid pole.

Portal of exit

Skin and nasal mucosa are main portal of exit of M.leprae, the latter is most important one. [32] Other portal of exit are breast milk and female genital mucosa.[33]

Portal of entry

Respiratory route and broken skin are the two main portal of entry. Bacilli may also enter through gastrointestinal tract and as transplacental transmission.[38]

Mode of transmission:[15,31]

- Inhalation(Droplet infection) – main mode of transmission
- Skin to skin contact
- In utero transmission
- Ingestion of Breast milk
- Inoculation following trauma
- Transmission through insects

INCUPATION PERIOD

The minimum incubation period reported is as short as a few weeks and this is based on the very occasional occurrence of leprosy among young infants. The maximum incubation period reported is as long as 30 years. However, average incubation period is 5 – 7 years.[15]

VACCINATION

Prevalence of leprosy is 2 times more in non-vaccinated children than vaccinated children. BCG vaccination provide 50% protection among contact children.[35]

IMMUNOLOGY

The clinical manifestations of Leprosy are highly influenced by the immune response of the subject against M.leprae. Immune response of the host was first pointed out by Mitsuda in 1954, he showed that intradermal injection of killed bacilli led to a skin reaction 3-4 weeks later with erythema and swelling at the site. Such reaction was observed only in Tuberculoid patients and not in Lepromatous patients. This reaction was indicating that the inflammatory response was dependant on host immune response.[36]

Later, Dharmendra showed that a lipid free soluble factor from the bacilli also produced a reaction in the shorter time period of 48- 72 hours.[36]

Mycobacterium leprae is an obligate intracellular parasite that grows inside macrophages and Schwann cells. In addition to macrophages and Schwann cells, other antigen presenting cells like dendritic cells, langerhans cells and keratinocytes play an important role in the presentation of M.leprae antigens to T helper cells for induction of immunity in the host.

The immunity in leprosy can be classified into: cell-mediated and humoral immunity. Cell-mediated immunity, expressed by T cells, is the determining factor in restricting the growth of bacilli and is responsible for building resistance against infection. In advanced stages of the disease, infection leads to extensive B cell proliferation, resulting in a state of increased humoral immunity with high antibody titer.

SPECTRAL MANIFESTATION OF THE DISEASE

Leprosy manifests in various forms depending on the host immunity. The two poles are the tuberculoid (TT) and lepromatous (LL) types. Towards the TT pole, the host macrophages are able to kill M.leprae, whereas towards the LL pole M.leprae grows abundantly in

these macrophages. There is an inverse co-relationship between the bacterial index/antibody levels and CMI in the spectral manifestation of the disease.

Ridley and Jopling classification was based on clinical, histological, immunological, and microbiological parameters and classified into the following five forms: TT, borderline tuberculoid (BT), midborderline (BB), borderline lepromatous (BL) and LL. In addition to these forms, there is an early stage of the disease, designated as indeterminate leprosy, presenting as vague anaesthetic patches, in which only a few inflammatory cells were seen.[37]

HUMORAL IMMUNITY

SPECIFIC ANTIBODY RESPONSE

levels of all the immunoglobulins (IgG, IgA, IgM and IgE) were seen in LL patients than in normal or TT individuals.[38]

Many autoantibodies were produced in Lepromatous leprosy patients like Cryoglobulin, Rheumatoid factor, C- reactive protein and false positive biological test for syphilis due to cardiolipin. These antibodies are not seen in Tuberculoid cases.

The cell wall of Mycobacterium leprae protects against these specific antibodies.

Specific serological assays such as phenolic glycolipid- (PGLI) based enzyme linked immunosorbent assay (ELISA)[39] and 35kDa based competitive inhibition assay were useful in monitoring patients under treatment and correlate well with their BI.[40,41] These are also useful in diagnosing cases of relapse. Although these tests are positive in 90% to 100% of BL/LL forms, they are not able to identify more than 40% to 60% of the cases of TT/BT leprosy, and therefore are not useful in diagnosing early leprosy.

Recently, a test developed as ML-Flow test has been claimed to be useful in diagnosing incubating leprosy in a household contact population in Thailand.[42]

ANTIBODIES AGAINST OTHER ORGANISMS

Lepromatous patients often show high antibody levels against antigens of Candida albicans, Salmonella typhae[43] and tetanus toxoid. In the lepromatous stages not only are the antibody levels to M. leprae raised, but antibodies to other opportunistic organisms are also increased, indicating a state of an over all activation of B cells. But, the

humoral immunity does not play any role in protecting the host against M. leprae infection.

CELL MEDIATED IMMUNITY

T-cell mediated immunity is protective immunity in leprosy. In lepromatous leprosy, there is unlimited growth of M. leprae in skin tissue, nerves and mucous membranes due to the selective unresponsiveness (anergy) of the T lymphocytes to M. leprae. A generalized depression of CMI in LL was observed. In the peripheral blood of LL patients, T cells are neither reduced in number, nor are there any changes in CD4+/ CD8+ T cell ratios.[44] These observations prove that there is no generalized depression of the T cell immunity, even in the advanced stages of the disease.

The specific CMI response has been determined by assessing skin delayed type of hypersensitivity(DTH) in patients. Although the lepromin test is not a diagnostic test, it has considerable prognostic value and provides confirmatory evidence for classification of the disease.[45] The test is usually strongly positive in most TT/BT patients. It is negative in BL/LL patients, but tends to become positive during a reversal reaction. In contrast, TT/BT patients during downgrading reactions may show a negative reaction.

T-LYMPHOCYTES

T-Lymphocytes count is reduced in all type of leprosy. Reduction is maximum in Lepromatous patients and minimum in Tuberculoid patients.

B-LYMPHOCYTES

There is increase in absolute number of B-Lymphocytes.

MACROPHAGES

Failure of macrophages to cope effectively with M.leprae is a main characteristic feature of Lepromatous leprosy. This is due to failure of T-cells to respond against M.leprae antigens and to secrete the macrophage activating lymphokines.

Macrophages from LL patients showed alteration in the surface property after phagocytosis of bacilli and unable to process the M.leprae resulting in inability to initiate the cell mediated immunity.

CLASSIFICATION[46,47]

DANNIELSSEN AND BOECK(1848)

1. Nodular
2. Anesthetic

NEISSER (1903)

1. Lepra tuberosa
2. Lepra cutanea
3. Lepra nervorum

PAN AMERICAN (1946)

1. Tuberculoid
2. Lepromatous
3. Un characteristic

MADRID (1953)

1. Lepromatous type(L)

- Macular
- Diffuse
- Infiltrated
- Nodular
- Pure neuritic

1. Tuberculoid type(T)

- Macular(Tm)
- Minor tuberculoid(Tt)
- Major tuberculoid(TT)

- Pure neuritic(Tn)

2. Indeterminate group(I)

- Macular(Im)
- Pure neuritic(In)

3. Borderline group(B)

- Infiltrated
- (Others?)

REVISED INDIAN CLASSIFICATION(1981)

1. Tuberculoid
2. Borderline
3. Lepromatous
4. Indeterminate
5. Pure neuritic

RIDLEY AND JOPLING (1962) [48]

1. Tuberculoid (TT)
2. Borderline tuberculoid(BT)
3. Borderline Borderline(BB)
4. Borderline Lepromatous(BL)
5. Lepromatous(LL)

WHO CLASSIFICATION(1998)

1. Paucibacillary single lesion leprosy(SLPB)
2. Paucibacillary leprosy(PB)
3. Multibacillary leprosy(MB)

PB

- 1– 5 skin lesions
- No nerve / only one nerve
- Skin smear negative at all sites

MB

- 6 and above skin lesions
- More than one nerve irrespective of number of skin lesions
- Positive skin smear at any site

CLINICAL FEATURES

There is wide variation in the clinical presentation of leprosy; in some persons the disease involves only one peripheral nerve or causes a single skin lesion, while in others it produces countless nodules and other types of skin lesions, with polyneuritis and damage to vital organs, such as eyes, larynx, bones and bones.These clinical presentations are depends on the immune status of an individual.[49]

CARDINAL SIGNS [50]

1. Hypopigmented or erythematous skin lesion with definite loss / impairment of sensation

2. Thickening of peripheral nerves with sensory impairment

3. Skin smear positive for acid-fast bacilli

1. SKIN LESIONS

Skin lesions may be single or multiple approximately 90% of the leprosy patients had skin lesions and 79.5% had skin lesion only.[51]

Hypopigmented or erythematous patches / plaques are the most common presentations in leprosy patients, along with sensory loss is specific for leprosy. Skin lesions should be examined for number, size, shape, margin, surface, symmetry, cutaneous nerves over the patch and sensation, includes temperature, light touch and pain.

The specificity of the diagnosis based on this is reduced in multibacillary cases because the lesions can be less distinct and less anesthetic. The sensitivity of this single criteria was 70% for all patients, almost 30% of leprosy patients may be missed.[52]

2. ENLARGEMENT OF PERIPHERAL NERVES

Leprosy is one of the most common cause of nerve enlargement. The most commonly involved nerves are superficial nerve trunks; ulnar, common peroneal and greater auricular are frequently affected in that order. Other nerves like median, radial, posterior tibial, facial and cutaneous nerves like radial cutaneous, supraclavicular, supraorbital and sural nerve are also felt.

Apart from the nerve trunks and the cutaneous nerves there may be enlargement of superficial nerves supplying the macule is of great diagnostic significance,more common in tuberculoid patch.

While examining the nerves following features are observed:

- No. of nerves enlarged
- Size of the nerves
- Symmetrical appearance
- Tenderness
- Extent of enlargement
- Nodular thickening or abscess along the course

False Positive findings may occur because of non-specific enlargement of nerves seen in heavy manual workers and other disease

conditions like neurofibromatosis, amyloidosis. To improve the specificity of the diagnosis of leprosy, besides thickened nerves, one other diagnostic sign such as typical skin lesion with sensory impairment is recommended.[53]

3. SKIN SMEAR

This is more specific cardinal sign for leprosy with the specificity of 100%.

SITES: Earlobe is the most common site, as it yield maximum bacilli. Other sites are forehead, cheek, chin, arm, thigh, buttock and from the patch. At early stage bacilli is demonstrated from nasal smear and pulp of fingers.[16,54]

METHODS: There are two methods of skin smear technique. They are snip method and slit method. In snip method small portion of skin is removed and crushed before staining. In slit method, the ear lobe is cleaned with spirit and then is pinched tightly between thumb and index finger for few minutes. An incision is made measuring 5mm in length and 3mm in width by using Bard Parker blade(No.15). Then scraping is taken from the cut surface. A smear is made on the glass slide with a diameter of 0.7 to 1 cm.[16]

The slides are stained by Ziehl-Nielsen's technique. Following indices are noted by microscopic examination of slides.

INDICES[16]

A. Bacterial Index(BI)

This indicates the number of bacilli seen in an average microscopic field. Minimum of atleast 25 microscopic fields are examined. In this method both live and dead bacilli are counted.The index is recorded as follows:

6+ is Many clumps of bacilli in an average field(over 1000)

5+ is 100 – 1000 bacilli in an average field

4+ is 10 – 100 bacilli in an average field

3+ is 1 – 10 bacilli in an average field

2+ is 1 – 10 bacilli in 10 fields

1+ is 1 – 10 bacilli in 100 fields

b. Morphological Index(MI)

In this living bacilli are counted after counting 200 bacilli and given as percentage.

Features of live bacilli are:

- Parallel surface
- Rounded ends
- Uniform staining.

MI is more specific than BI.

c.SGF Index

Solid, Fragmented and Granular index. The value is:

2, if they are numerous

1, if they are few(1-20%)

0, if less than 1%

EARLY SIGNS OF THE DISEASE

- Hypopigmented / erythematous, anesthetic / hypoesthetic skin lesion.Tuberculoid lesions are well defined hypopigmented/ erythematous anesthetic patch/ plaque. Early lepromatous lesions are vague, ill defined coppery or hypopigmented
- Numbness or feeling of pins and needles or crawling of ants or tingling sensation / weakness in fine movements.
- Burns resulting from contact with hot objects.

- Appearance of spontaneous blisters and ulcers.
- Rarely features of reactions like fever, joint pain,erythematous tender skin lesions and edema of hands and feet.

Other features should be examined are:

- Ear lobe infiltration
- Madarosis
- Bilateral gynaecomastia
- Bilateral pedal edema
- Hepatosplenomegaly
- Lymph nodes
- 5^{th} and 6^{th} cranial nerves for lagophthalmos and corneal sensation
- Muscle weakness

INDETERMINATE LEPROSY

In 20 to 80% of patients intermediate leprosy is the first presentation of the disease. It is developed before the host develops immune response to M.leprae, which is recognized only by nonspecific defense mechanisms .[55]

This type is more common in children, skin lesions consist of medium to large sized hypopigmented patch, often seen on the external aspect of thigh , face, extensor aspects of limbs with vague edges and some loss of sensations. Hair growth and nerve functions are rarely affected. Occasionally dryness and wrinkles may be seen over the lesion. Nerve thickening is not commonly seen, but sometimes thickened. Lepromin test may be strongly positive or weakly positive or negative.[56,57]

Skin biopsy is done to confirm the Indeterminate leprosy. AFB are not usually demonstrable, but occasionally can be demonstrated within cutaneous nerves in biopsy.

This type of leprosy may undergo self healing. About 30% of indeterminate type may progress into determinate type, especially towards lepromatous pole. Progression towards tuberculoid pole is indicated by increased anesthesia and well defined margin , lepromatous pole is indicated by appearance of multiple new lesions. The prognosis with treatment is good, lesions heal without any neurological or reactional sequelae.

TUBERCULOID LEPROSY(TT) [49, 55, 58]

Tuberculoid leprosy is a stable and benign type of leprosy; Clinically presents as well defined erythematous elevated lesions with involvement of peripheral nerves. Nerve involvement is usually unilateral and asymmetrical, it occurs due to extension of bacilli from or through cutaneous nerve branches. This may present as purely neural with pain and swelling of nerves, tingling sensation, loss of sesation, muscle weakness and paralysis.Alternatively skin lesions may appear without nerve involvement.

The skin lesions are usually single but may be up to three in number , often eythematous plaques, less commonly hypopigmented macules.The typical skin lesion is well defined , raised and a tendency to central flattening. The surface is dry, anaesthetic, hairless and sometimes scaly with size may be over 10 cms in diameter.

The skin lesions are usually appear on the face, buttocks, lateral aspect of extremities and scapula. The dryness and sweat loss over the lesion is due to autonomic nerve damage in the lesion. Another characteristic feature is cutaneous nerve thickening which is supplying the affected area and palpated near the margin of the lesion. Usually single nerve trunk is thickened which may be in the vicinity of skin

lesion for example a thickened ulnar nerve if the lesion is over the forearm . Nerve thickening may be smooth or irregular and rarely cystic swelling of nerve and calcification may occur. On slit skin smear examination no AFB is seen and strongly positive Lepromin test.

Tuberculoid leprosy is subdivided into major and minor tuberculoid forms.[59]

Major tuberculoid

Lesions are very large and numerous with well defined margin . They are erythematous, uniformly raised plaques with severe nerve involvement.The lesions are frequently seen over the face and also invade the immune zones like scalp, axilla, palms and soles. Cutaneous nerves are often enlarged and thickened nerves may persist for long time even after the patch has regressed.

Minor tuberculoid

The skin lesions are usually small, hypopigmented and moderately elevated at the margin. The characteristic papules are seen at the periphery which proceed to rapid clearing. Usually this type is not associated with nerve enlargement, cutaneous nerve in vicinity of skin lesion may be enlarged.

Tuberculoid leprosy may heal itself even without treatment, so the prognosis is good. Rarely subpolar tuberculoid lesions may downgrade into next spectrum. The anesthesia over the lesion may persist even after treatment.

Nodular leprosy in children is a benign clinical variant of tuberculoid leprosy that affects the breast feeding infants and children. This is considered to be a manifestation of allergy and congenital immunity to M.leprae. Lesions are characterised by indurated nodules, papulo nodules, wheal like lesions, macules, solitary infiltrations and lichenoid lesions usually over the cheeks, limbs and buttocks. They may resolve spontaneously without any nerve damage or deformity.

BORDERLINE LEPROSY

Borderline leprosy is also known as dimorphous leprosy, occurs in the spectrum between tuberculoid and lepromatous poles. Most of the deformities and disabilities are seen in borderline leprosy. This is immunologically unstable form and therefore may move in either direction. Tendency for lepra reaction is more in this group. Borderline leprosy is further classified into BT, BB, BL based on symmetry and distribution of skin lesion, border, sensory impairment,

sweating, hair growth, nature and extent of peripheral nerve involvement, mucosal involvement and SSS results.[60]

BORDERLINE TUBERCULOID(BT)

This is the most common type of leprosy. The skin lesions of BT resembles those of tuberculoid leprosy. The number of skin lesion is more than TT, upto 10 or more and asymmetrically distributed. They vary in size and may cover the whole limb. The lesions are well defined and raised in some part, flat and vague in another. Hypopigmentation, dryness, scaling, anesthesia and pebbling are less pronounced than in TT.

Pseudopodium may be seen, which is a small extension from the lesion at one edge. The most characteristic satellite lesions may be seen. Peripheral nerves are irregularly enlarged and in asymmetrical pattern. Nerve damage is severe and widespread. Anesthesia and motor deficit may be found at the time of presentation. Nerve damage may progress even after initiation of antileprosy treatment.[49]

BT leprosy with large hypopigmented macule and nerve involvement is sometimes called maculoanesthetic or low resistant tuberculoid leprosy(macular tuberculoid). In this type the lesions are large and asymmetrical in distribution and more commonly seen over

face, buttock, lateral aspect of extremities, and scapula.The lesions are hypopigmented with well defined edges and dry, rough surface and show some degree of loss of sweating and sensation.[61]

The striking feature of BT is the occurrence of type 1 reaction. If untreated, repeated bouts of reactions may produce progressive nerve damage, paralysis and deformity. The lepromin test is usually weakly positive. The bacilli are scanty or absent in slit skin smear.

BORDERLINE BORDERLINE(BB)[58]

This is most unstable form of the spectrum and very rarely seen. Because of immunological instability,the disease rapidly moves into BT or BL. Mid-borderline disease is mostly downgrades towards the lepromatous pole if untreated. The lesions are more in number usually more than 10 in number but not as many as lepromatous leprosy and vary in size and shapes. The lesions may be macules, papules, plaques, circinate lesions or nodules.

- Macules: These are hypopigmented in dark skinned people and erythematous in fair people, numerous, less well defined and tendency towards symmetry.

- Plaques: Erythematous or coppery.

- Annular lesions: These are circular or oval in shape with well defined outer and inner edges. The skin in the centre of the lesion may be normal in colour.

- Punched out lesions: These are characteristic of BB leprosy. Lesions are erythematous plaques with ill defined, sloping outer edge and a punched out centre with well demarcated edge.

- Bizarre lesions: These are large lesions with geographical appearance.

- Nodules: Occasionaly nodules over ear and chin may occur.

Nerve damage is variable. If the patient is downgrading from BT, nerves may be multiple and asymmetrically enlarged. If the patient is upgrading from BL to BB, the nerves may be symmetrically enlarged.

TABLE 1

RIDELY AND JOPLING CRITERIA

S.NO	CRITERIA	TT	BT	BB	BL	LL
01	No.of lesions	1 - 3	4-10	11-20	>20	Multiple
02	Size	Variable	Variable	Variable	Variable	small
03	Surface	Very dry	Dry, rough	Smooth, soft, slightly shiny	Smooth, soft, slightly shiny	Smooth, soft, slightly shiny
04	Margins	Well defined	Well to ill defined, mostly well defined	Well to ill defined	Well to ill defined, mostly ill defined	Ill defined
05	Central healing	+	+/-	+/-	+/-	-
06	Satellite	None	+	+/-	-	-
07	Sensation in the lesion	Absent	Moderately – markedly diminished	Slightly - moderately diminished	slightly diminished	Not affected
08	Loss of hair over the lesion	Absence of hair	Markedly diminished	Moderately diminished	slightly diminished	Not affected
09	Loss of sweat	+	+/-	+/-	+/-	+/ -
10	Symmetry	-	-	-	+/-	+
11	Local cutaneous nerves	+	+/-	-	-	-
12	Peripheral nerves	Nerves close to the skin lesion are affected	Multiple nerves are affected	Multiple nerves are affected	Multiple nerves are affected	Multiple nerves are affected
13	Other systems	Not involved	Not involved	Not involved	Mild	Severe
14	AFB stain-BI	0 to 1+	0 to 2+	2+ to 3+	4+ to 5+	5+ to 6+
15	Lepromin test	+++	++	+	-	-

BORDERLINE LEPROMATOUS(BL) [61, 62]

This type of leprosy shows more of lepromatous features but still shows some tuberculoid features. The skin lesions are usually numerous, small, vague, round or oval macules about 2-3 cm in diameter. They may be erythematous, hypopigmented or shiny and starts with vague macules,initially a small group but soon become widespread over the trunk. The macules are smaller and not so symmertically distributed. When the disease progress papules, nodules and plaques may develop and some of the macules become infiltrated they appear as 'spots of grease' on a well paved road, especially over the face and ears.

Peripheral nerve involvement occur sooner than in lepromatous leprosy. Signs of nerve damage like decreased sensation, sweating and hair growth start soon. Eyebrows are either normal or partially involved. Glove and stocking anesthesia are not developed till late in the disease and eyes, oral cavity and testes are also normal.

Many patients of BL are downgraded from BT. Associated large lesions with some central healing indicates downgrading of disease from higher spectrum.Type 2 reactions are more common in BL patients. Type 1 reactions, though uncommon, may occur in this spectrum.

Lepromin test is negative in this patients.

The prognosis of BL leprosy is variable.If the disease starts as BL and treated early, the prognosis will be good. If the disease is downgraded from BT to BL, the nerve damage and development of reactions will be more, which further complicate neuritis and disabilities.

LEPROMATOUS LEPROSY(LL) [49,61,62]

Lepromatous leprosy occurs in persons with low level of immunity against M.leprae. After enter into the body the bacillus multiplies and spread in the skin, mucous membranes, nose, eyes, liver, spleen, lymph nodes,testes and adrenals. The bacilli does not enter into the brain and spinalcord,also not travel beyond the bifurcation of trachea.

Glove and stocking anesthesia, corneal anesthesia, madarosis, leonine facies and various systemic involvement are characteristic. The skin lesions are macular, papular,infiltrated and nodular. Ulcerative lesions may also occur rarely. The early lesions are usually small macules, innumerable in number, widely disseminated and symmetrically distributed. They are ill defined, erythematous and slightly hypopigmented with shiny and moist surface. As they progress

the entire body surface will be involved. The early lesions are not anesthetic. Sensation is usually unimpaired in early lepromatous lesions, but sweating may be diminished.

If the patient is not treated the skin become infiltrated, and gives waxy appearance. Skin creases will be lost and erythema increases. The lesions are distributed on the face over forehead, zygoma, chin and ear lobes, and on the limbs over the cooler dorsal areas, fore arm, back of the hand, external surface of the lower legs. There is clinical evidence of nerve damage present in this stage. First there is loss of sensation over dorsum of hands, forearms and lower legs. The area of sensory loss spreads slowly until all skin is anesthetic except scalp, axillae and groin.

LL with infiltrated lesions presents as three forms: Diffuse, Infiltrated and Nodular forms.

DIFFUSE LL

This type occurs as a result of coalescing of the numerous vague macules. The skin looks shiny with slight infiltration. Eyebrows may show thinning or loss of hair, but loss of eyebrow is late sign.

INFILTRATED LL

This is more advanced stage of macular LL with visible infiltration. The lesions will appear shiny, erythematous and raised. This may be a sign of advancement of diffuse LL.

NODULAR LL

This type is characterised by development of multiple nodules all over the body. In early stage, nodule appear over the ears then the disease advances they appear over buttocks,extremities, over joints and genitals. This infiltrated plaques and nodules over face accentuate the skin folds producing 'Leonine facies'. At early stage the nodules are mobile in the subcutaneous tissue, but later they are fixed and liable to ulcerate.

There is gradual onset of sensory and autonomic nerve damage in the cooler parts of the body, it may be difficult or impossible to find clinical signs of damage to the large peripheral nerves until the disease is well advanced. The peripheral nerves first become enlarged and firm, then hard and fibrosed, at sites of predilection, symmetrical. The muscles of hand and feet are affected directly as well as through the peripheral nerves. So, muscle weakness of the hands appear early in disease. The peripheral anesthesia may be extensive and is accompanied

by anhidrosis with compensatory hyperhidrosis of face, trunk and axillae.

Hair is lost in all lesions, especially over the face. Scalp hair usually spared. Very rarely in advanced disease, scalp may be involved, there may be residual hair growing only over the course of the arterial supply to the scalp called ‘Leprous alopecia’.

Nail growth may be affected late in the course of disease. Nail plate become thin and lusterless, shrunken, narrowed, ridged and curved. The relevant digits are narrowed because of bone atrophy and retain the nail in a shrunken form.

Nasal mucosal involvement is seen in 80% and carries a high risk of infectivity. Nasal symptoms may occur earlier than appearance of skin lesions. Patients may develop nasal stuffiness or block, mucopurulent discharge and epistaxis. The mucosa of inferior turbinate and nasal septum may be yellow, swollen and covered with crust. At late stage, destruction of nasal cartilage and perforation of nasal septum will produce nasal collapse. Patient rarely may develop anosmia, due to involvement of olfactory nerve. Nose blows are full of bacilli.

Involvement of larynx is a late manifestation and it may be fibrotic form or ulcerative form. This causes hoarseness of voice, stridor

and cough. Papules and nodules may be seen over mucosal surface of lips, palate, tongue and uvula. Palatal nodules may ulcerate and produce perforation of hard palate. Loosening or loss of upper central incisor teeth, along with nasal collapse is called ‘Facies leprosa’, this occurs due to atrophy of maxillary alveolar process and anterior nasal spine.

Eye involvement may be due to, direct infiltration of eye and surrounding tissues by bacilli or abnormal exposure of eye secondary to involvement of fifth and seventh nerves. Ocular manifestations are lagophthalmos, corneal anesthesia, corneal opacity, perforation, uveitis and blindness.

Involvement of internal organs, bones, liver, spleen, lymph nodes, kidney, adrenals and muscles may occur but testicular involvement is common. Gynecomastia may follow testicular atrophy.

Bone and joint involvement ranges from mild tenosynovitis to leprous osteomyelitis.

VARIENTS OF LEPROSY

1. Pure neuritic leprosy:[63]

Pure neuritic leprosy accounts for 5 to 10% of all patients with leprosy. Most of the patients are mononeuritic. This is characterized by

area of sensory loss in the absence of skin patch with or without motor deficit. This form of leprosy is seen most frequently in India and Nepal. Common age group is 20 to 40 yrs.

A spectrum of TT to BT is seen in histopathology of pure neuritic leprosy. The ulnar, median, common peroneal, posterior tibial, greater auricular and radial nerves are involved in the order of frequency. The cranial nerves 5^{th} and 7^{th} may also be involved.

2. Lucio's Leprosy:

Lucio leprosy is a diffuse, non nodular form of lepromatous leprosy, almost limited to Mexico. It was first described in 1852, by Lucio and Alvarado, and later by Latapi and Zomara in 1948. It presents as a uniform diffuse shiny infiltration of the entire skin and the appearance of the skin is waxy and shiny and in Mexico it is referred to as 'Lepra bonita; Beautiful leprosy'.

The eyelids are swollen and giving a sleepy, sad appearance. There may be numbness and edema of the hands or feet, nasal congestion, epistaxis, hoarseness of voice and madarosis seen; this may be mistaken for myxedema. Development of reaction in this type of leprosy is called Lucio phenomenon, which is characterized by multiple purpuric lesions evolving into ulceration.[64]

3. Localized Lepromatous Leprosy

This present as a single nodule or plaque with shiny and sloping margins. The biopsy may show a lepromatous histology and full of bacilli. The rest of the skin is normal and SSS are negative.

4. Lazarine Leprosy:[65,66]

Lazarine leprosy is an unusual manifestation of Borderline tuberculoid leprosy characterized by severe ulceration, seen usually in patients with malnutrition or other debilitating illness. These ulcers are deep up to the tendons or bones level and shows large numbers of bacilli. The ulceration is due to extreme cellular hypersensitivity. In addition to antileprosy drugs steroids are necessary.

5. Autoaggressive Hanseniasis:[67, 68]

This is seen in lepromatous leprosy or in borderline leprosy and the features resembling connective tissue diseases like SLE. The patients may present with fever, anorexia, asthenia, arthralgia, weight loss, neuralgia, photosensitivity, malar rash, erythema nodosum, and erythema multiforme-like skin lesions.

Generalized lymphadenopathy, orchitis, epididymitis, arthritis, nephritis, iritis, uveitis, and hepatitis may also be seen. In addition,

patient may have antinuclear antibodies in their serum. The antigen complexes of bacteria and autologous tissue stimulate B cells and also cause dysfunction of suppressor T Lymphocytes. It responds to thalidomide 100–300 mg/d in combination with anti-leprosy drugs.

6. Silent or Invisible Lepromatous Leprosy

There is no skin infiltration in this type and the patients are diagnosed incidentally when they develop nasal symptoms or peripheral anesthesia or type 2 reaction. The slit skin smear will be positive from all sites, but the patient may be asymptomatic.

7. Spontaneous Skin Ulceration:

Long-standing LL patients rarely may develop panniculitis like induration of the subcutaneous tissue or muscles and ulcers. This may occur over the anterior thigh, forearm, calf or triceps.

8. Histoid Leprosy:[69-71]

The term Histoid was introduced by Wade,in the year of 1960. This is an unusual variant of LL and is characterized by cutaneous / subcutaneous nodules and plaques on apparently normal skin with unique histopathological features and bacterial morphology. This is more common in males than in females and most common age group is

10-84 years. It occurs in the patients with dapsone resistance, dapsone monotherapy, irregular and inadequate treatment.

The lesions are reddish, dome shaped or oval, shiny, succulent, protuberant nodules mostly over the extensor aspects of the extremities, buttocks, back, face and bony prominences such as around the elbows and knees. The ears are unaffected. Occasionally, lesions may simulate molluscum contagiosum .

A slit skin smear shows abundant AFB occurring in clusters, but absence of globi. The bacilli are longer with tapering ends compared to normal M.leprae. This will be treated with MB-MDT for the duration of two years.

PATHOGENESIS AND HISTOPATHOLOGY

M.leprae is an obligate intracellular parasite within the macrophages and Schwann cells. The bacilli show preference for growth in cooler regions of the body. It still cannot be cultivated in vitro. The G-domain of the laminin α2 chain in the basal lamina of Schwann cells , α-dystroglycan and the laminin receptor are the receptor complex on the Schwann cells. The ligands on the surface of M.leprae which bind to this complex are PGL-I and a 21 kDa surface protein.[72,73]

Nerves are the only sites where the bacilli are demonstrated in the earliest lesion. Later the bacilli are demonstrated at the dermoepidermal junction. As per the order of importance, the organisms are seen in nerves, neurovascular bundles, subepidermal zone, smooth muscles, sweat glands and their ducts.[74]

In TT a vigorous cellular response occurs to limit the disease to the well-defined skin patches or nerves. The lesions are infiltrated by $CD4^+$ T lymphocytes, which form well defined granulomas containing epithelioid and multinucleate giant cells around dermal nerves. Cellular immunity is confirmed by in vitro lymphocyte responses to M.leprae antigens or by skin test reactivity. Spontaneous fluctuations in the immune response are responsible for reversal reactions and erythema nodosum leprosum.

There is absence of M.leprae-specific cellular immunity in Lepromatous leprosy, and this will causes uncontrolled proliferation of the bacilli with extensive infiltration of the skin and nerves. Histologically, the dermis is filled with foamy macrophages and a scattering of $CD4^+$ and $CD8^+$ lymphocytes, but absence of organized granulomas. There is progressive reduction in cellular responses is seen

in Borderline leprosy, which is associated with a greater bacillary load, more frequent skin and nerve lesions.

SKIN BIOPSY [75]

Importance of skin biopsy

- To confirm the diagnosis
- To classify leprosy
- To identify the complications like reactions
- To help in the management

Site

In indeterminate leprosy the biopsy should be taken from the middle of the lesion, where the lesion is active. If multiple lesions are present, the most active lesion will be selected and biopsy is taken from the edge of the lesion.

Size

The elliptical piece of skin with size of 1.5 cm long and 0.6 cm wide with the depth of dermis and subcutis will be taken.

Fixatives

- Lowy's fixative (FMA)
- Formaldehyde(40%) - 100ml
- Mercuric chloride - 20 g
- Glacial acetic acid -30 ml
- Distilled water -1000 ml

The biopsy specimen should be kept in this solution for 2 hrs and then transferred to 70 % ethyl alcohol, in which it can be stored for long time. The following stains are done:

- Haematoxylin & eosin stain
- Fite-Faraco stain
- Gomari methanamine silver stain
- Immunochemical stain
- S-100 stain

Of all these staining procedures H & E stain and Fite-Faraco stains are most commonly used.

FITE-FARACO STAINING PROCEDURE: [76]

- De paraffinize sections with xylol and liquid paraffin mixture (2 parts of xylol and 1 part of liquid paraffin). Two changes of 12 min each.
- Drain, wipe excess of oil and blot to opacity. The residual oil helps to prevent shrinkage and injury to sections. It also prevents removal of acid-fast material from the organisms.
- If the tissue is fixed with fixatives containing mercuric chloride, do the additional two steps:
    - Treat the section with Lugol's iodine for 5 min and wash in water.
    - Bleach the sections with 5% hypo (sodium thiosulfate) for 5 min and wash in water for 5 min.
- Stain with Ziehl–Nielsen carbol fuchsin solution for 30 min at room temperature.
- Wash in tap water until all the excess stain runs out.
- Decolorize slides individually with 5% sulfuric acid for 10 min.
- Wash in tap water for 10 min.

- Counterstain with Harris' hematoxylin for 15 sec.
- Wash in running water for 5 min.
- Blot and dry.
- Dip in xylol.
- Mount in gum dammar or DPX mounting medium

Hematoxylin and Eosin stained sections of skin biopsies will be examined for

a) Epidermal atrophy

b) Epitheloid and Macrophage Granulomas

c) Number and Distribution of Lymphocytes, Histiocytes and Foam cells

d) Infiltration of Nerves, Blood vessels and Adnexa

e) Grenz Zone.

Sections stained with Modified Fite's stain will be examined for Acid Fast Bacilli in all cases. Histopathological findings will be graded into Polar Tuberculoid(TT), Borderline Tuberculoid(BT), Mid-Borderline(BB), Borderline Lepromatous(BL), Polar Lepromatous(LL) based on Ridley and Jopling Scale.

TUBERCULOID LEPROSY(TT) [75-78]

- Epidermis is usually thin
- Rete ridges are flattened
- Subepidermal free zone (Grenz zone) is absent, which is invaded by foci of inflammatory cells.
- Dermis shows tuberculoid granuloma which consist of collections of epithelioid cells with few Langhans giant cells surrounded by a well-formed rim of lymphocytes, Caseation is usually absent. The granuloma may extend from the deeper dermis in to the papillary layer of the dermis and causes erosion of the epidermis and atrophy.
- Epitheloid granulomas are also seen adjacent to blood vessels, sweat glands, hair follicles, and sebaceous glands.
- Dermal nerves are surrounded by well-formed epitheloid granulomas with extensive destruction of nerves are seen.

Acid fast bacilli

Absent; non viable bacilli may sometimes present

BORDERLINE TUBERCULOID(BT) [74,75]

- Atrophy of epidermis.

- Clear subepidermal zone may be seen,but at some points spur of granuloma may enter the epidermis.

- The granulomas are poorly formed and composed of collection of epitheloid cells, Langhan's giant cells and lymphocytes. In early lesion the granulomas are branching and project as spur along the neurovascular bundle.

- Nerves are swollen with granuloma and the infiltration of lymphocytes in perineurium may cause slight lamination.

AFB stain: BI is around 0 to 2+

MID BORDERLINE (BB) [75]

- Epidermis is atrophic.

- Clear subepidermal zone is seen.

- Dermis contains diffuse granuloma which consist of admixture of almost equal number of epitheloid cells and macrophages. Lymphocytes are less in number and scattered in granuloma.

- Giant cells are absent, this will help to differentiate it from BT.

- Usually some amount of intercellular edema is present.

- Nerves are infiltrated by granuloma, but not completely destroyed.There is lymphocytic infiltration and reactive proliferation of perineurium.[79]

AFB: BI is 3+ to 4+

BORDERLINE LEPROMATOUS (BL)

- Atrophic epidermis is separated from the granuloma by clear subepidermal zone(Grenz zone).

- Poorly formed granuloma is seen in dermis, which consists predominantly macrophages with solitary clump of epitheloid cells. Lymphocytes and plasma cells may also be seen. Some of the macrophages may show foamy changes.

- There is concentric perineural proliferation giving rise to onion peel appearance. Perineurium is infiltrated by many macrophages and lymphocytes.

- Clumps of AFB are seen within the macrophages, perineural cells, endothelial cells, Schwann cells and arrector pili muscle.

AFB stain: Plenty of bacilli with small globi will be seen. BI is 4+ to 5+

LEPROMATOUS LEPROSY (LL) [75]

- Epidermis is thin and atrophy.
- Rete ridges are completely flattened.
- There is clear subepidermal zone.
- Dermis shows macrophage granuloma. Initially most of the macrophages have pink and granular cytoplasm, later in old lesions the cytoplasm becomes foamy and vacuolated (Virchow cells or Lepra cells).
- Focal collections of plasma cells and few lymphocytes are distributed in the lesion.
- Cellular infiltrates are seen as a small focal cluster in early lesions, as the disease progress these clusters merge together to form a band of infiltrate in the dermis and may extend to subcutaneous fat. Piling of macrophages and other inflammatory cells lifts up the overlying skin producing plaques and nodules.
- Nerves are also infiltrated by macrophages. Reactive proliferation of perineurium is minimal.

AFB stain: Clumps of bacilli are seen in macrophages, perineurium, endothelial cells, Schwann cells, arrector pili muscle, sweat and sebaceous glands and hair follicles.

BI is 5+ to 6+

INDETERMINATE LEPROSY (IL) [75, 80, 81]

These lesions are difficult to diagnose clinically, and may require histo-pathological examination to confirm the diagnosis. The histopathological changes are minimal and may be missed unless the biopsy is adequate, including some amount of subcutis.

- No significant changes in epidermis but may show areas of atrophy.
- The dermis may consist of a mild perivascular and periadnexal infiltrate of histiocytes and mainly lymphocytes.
- The dermal nerves are thickened and infiltrated by lymphocytes. Schwann cell hyperplasia may be seen.
- The presence of AFB in any one of the following locations confirms the diagnosis- immediately underneath the epidermis, arrector pili muscle, nerve bundles or in a macrophage.

A presumptive diagnosis of leprosy can be made, even in the absence of M.leprae, if the inflammation of nerve is accompanied by

clinical features of nerve involvement, such as sensory loss. In the affected nerve, some fascicles may show inflammation while others may be spared , so examination of multiple consecutive sections are important.

It is important to examine at least 10–15 sections before ruling out the diagnosis of leprosy. The Fite–Faraco stain is recommended for demonstrating bacilli in tissues.

HISTOID LEPROSY [82-84]

- Atrophic epidermis.
- There is clear subepidermal zone.
- Circumscribed lesion is usually located in deep dermis or subcutis and is surrounded by pseudo capsule.
- The lesion is expansile in nature and consisting of spindle shaped histiocytes. Bacilli are arranged in parallel bundles aligned along the long axis of the histiocytes (Histoid habitus). These bacilli are longer than the normal lepra bacilli.
- Presence of foci of epitheloid cells in the lesion is known as tuberculoid contamination.

AIMS OF THE STUDY

- To study the epidemiological aspects of Leprosy like age, sex distribution etc.
- To study the various types of clinical presentation among the patients
- To study the Clinico-histopathological correlation in various spectrum.

MATERIALS AND METHODS

The prospective study was conducted at Outpatient Department of Dermatology in Rajiv Gandhi Government General Hospital, Chennai- 3 for a period of one year from October 2013 to September 2014.

A minimum of fifty patients of Leprosy belonging to all age groups and both sexes were randomly selected and included in the study after taking their consent. In each patients detailed history, thorough general and local examination was done as per the standard protocol followed for examining a patient with Leprosy. In all patients necessary investigations and Slit skin smear were done. Skin biopsy was done in all cases for histopathological study with patients consent.

INCLUSION CRITERIA

- Patients of both sexes proven to have Hansen's who had not taken any anti-leprosy treatment prior to visiting our OPD
- Patients who gave consent for Biopsy

EXCLUSION CRITERIA

- Patients who had already taken MDT in the past
- Patients not willing for Biopsy
- Pregnant women

HISTORY

Detailed history of age, sex, occupation and socioeconomic status was taken and presenting complaints like skin lesions, numbness, trophic ulcers and deformities were noted. In this study socioeconomic status of patients was divided into 3 categories based on kuppusamy's scale.

CLINICAL EXAMINATION

A detailed general examination was carried out in all the patients. Local examination of skin lesions was carried out with particular references to the number, shape, size, surface, margins, satellite lesions, supplying nerves, sensation, sweat loss, hair loss and trophic changes. All the peripheral nerves were palpated for enlargement and tenderness.

The patients were clinically diagnosed as Tuberculoid(TT), Borderline tuberculoid(BT), Borderline borderline(BB), Borderline lepromatous(BL), Lepromatous(LL).

ROUTINE INVESTIGATIONS

All patients were investigated routinely like Hb%, total count, differential count, ESR, Platelet count, bleeding time, clotting time and ELIZA for HIV.

SLIT SKIN SMEAR

Slit smear was taken for demonstration of Acid fast Bacilli. It was taken from 2 ear lobes and active lesion. Then the smear was allowed to dry and fixed by passing the slide over the top of a flame. The fixed smear was stained with Ziehl-Nielsen stain. The Bacteriological Index (BI) was calculated according to Ridley's scale.

PREPARATION OF REAGENTS

Carbol Fuchsin

- Basic fuchsin 2 g
- Phenol, melted 10 ml
- Alcohol 90% 20 ml
- Distilled water 170 ml

Weigh basic fuchsin and place in an Erlenmeyer flask, then add phenol and subsequently add alcohol and then add 10 ml of water. Shake to mix well, then add about 20–25 ml water. Shake until all the dye is dissolved. Then add the balance water and shake well. Filter it and store in a labelled and tightly stoppered bottle as a stock solution. Then fill labeled dropping bottles when needed for staining smears.

Sulfuric Acid

- Concentrated sulfuric acid 10 ml
- Distilled water 190 ml

Measure water and pour in an Erlenmeyer flask. Then measure acid and pour acid slowly down the side of the flask into the water. Never pour water into the acid. Then rotate to mix and then shake. The solution will become hot. When cool, pour diluted acid into a labeled tightly stoppered bottle. Store as a stock solution. Then pour into a labeled dropping bottle when needed for staining smears.

Acid Alcohol

- Concentrated hydrochloric acid 10 ml
- Ethyl alcohol 70% 990 ml

Pour acid gradually into alcohol stirring to mix. Store in screw capped labeled bottles and pour into dropper bottles as needed.

Methylene Blue

- Methylene blue 0.4 g
- Absolute alcohol 20 ml
- Distilled water 180 ml

Weigh methylene blue and place in a mortar. Then add 20 ml absolute alcohol and grind to dissolve. Then add 25–50 ml water and mix well. Then transfer with a pipette to an Erlenmeyer flask and then add the balance water. Shake well and filter. Then store in a labelled and tightly stoppered bottle as a stock solution. Then pour into a labeled dropping bottle when needed for staining smears.

ZIEHL-NEELSEN STAINING PROCEDURE

1. Place the slide with fixed smears on rods over a sink.
2. Flood with carbol fuchsin. Heat gently by passing a spirit lamp along the underside of the slides until a cloud of steam rises. Do not heat to boiling. Do not allow the stain to evaporate to dryness. Steam for 15 min.
3. Allow to cool. Wash in tap water.
4. Flood with 5% sulfuric acid. Let it stand for 3 secs.
5. Wash in tap water.
6. Flood with methylene blue (for counterstaining). Let it stand for 10 secs.
7. Wash in running water and allow to dry.

M.leprae is a acid-fast bacilli, is seen as pink coloured rods arranged in clumps.

HISTOPATHOLOGICAL EXAMINATION

Skin Biopsy specimen was obtained from all clinically diagnosed cases of Leprosy and was subjected to the following staining techniques

- ❖ Hematoxylin and Eosin stain
- ❖ Modified Fite's stain

Hematoxylin and Eosin stained sections of skin biopsies were examined for

- ❖ Epidermal atrophy
- ❖ Epitheloid and Macrophage Granuloma.
- ❖ Number and Distribution of Lymphocytes, Histiocytes and Foam cells
- ❖ Infiltration of Nerves, Blood vessels and Adnexa
- ❖ Grenz Zone.

Sections stained with Modified Fite's stain were examined for Acid Fast Bacilli. Histopathological findings were graded into Polar

Tuberculoid(TT), Borderline Tuberculoid(BT), Mid-Borderline(BB), Borderline Lepromatous(BL), Polar Lepromatous(LL) based on Ridley and Jopling Scale.

STATISTICAL ANALYSIS PLAN

Datas obtained were analysed using appropriate statistical package suggested by the Statistician.

OBSERVATION AND RESULTS

Age distribution

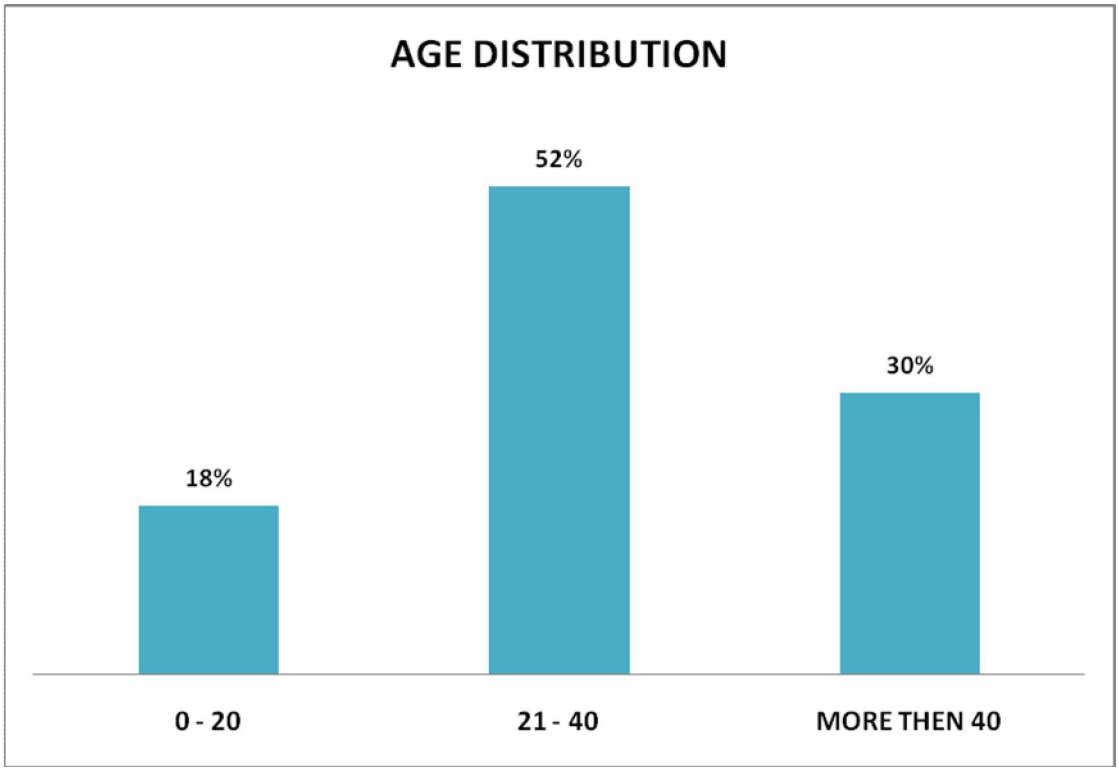
In our study, the youngest patient was 7 years old and the eldest was 65 years old.

The maximum number of patients(52%) showing clinical activity in this study belonged to the 21- 40 years age group whereas the least number of patients belonged to the less than 20 years age group.

TABLE 2 : AGE DISTRIBUTION

Age	Frequency	Percent
0 – 20	9	18.0
21 – 40	26	52.0
MORE THEN 40	15	30.0
Total	**50**	**100.0**

FIGURE 1: AGE DISTRIBUTION



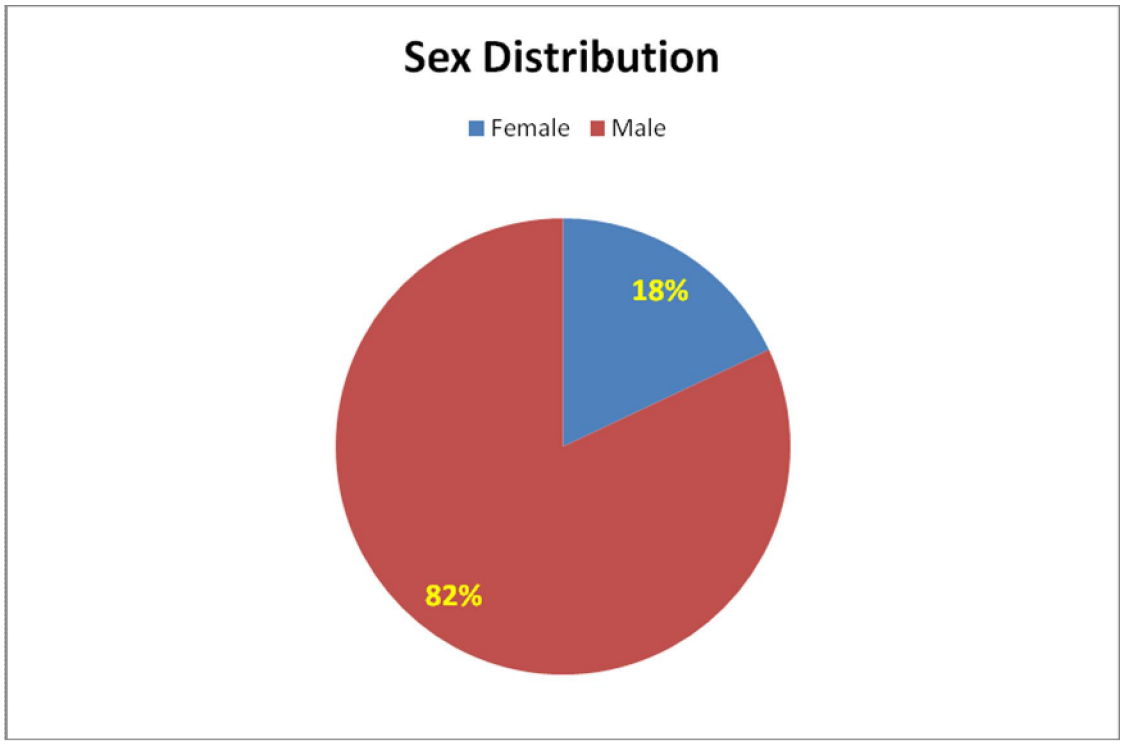
Sex distribution

In the present study, male patients comprised 82 % and female patients 18 % of the total patients.Male to female ratio was 4.5 : 1

TABLE 3: SEX DISTRIBUTION

Sex distribution	Frequency	Percent
Female	9	18.0
Male	41	82.0
Total	**50**	**100.0**

FIGURE 2: SEX DISTRIBUTION



Occupation

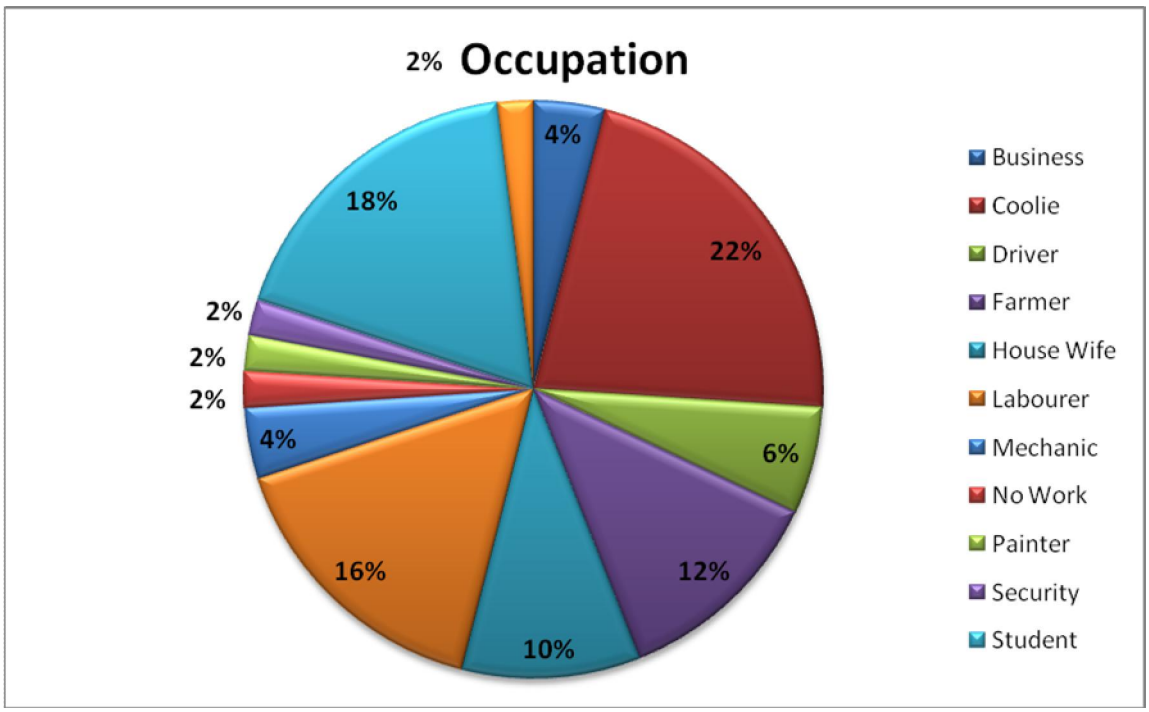
In our study maximum number of patients were coolies (22%).

TABLE 4: OCCUPATION

Occupation	Frequency	Percent
Business	2	4.0
Coolies	11	22.0
Driver	3	6.0
Farmer	6	12.0
House wife	5	10.0
Labourer	8	16.0
Mechanic	2	4.0
No work	1	2.0
Painter	1	2.0
Security	1	2.0
Student	9	18.0
Tailor	1	2.0
Total	50	100.0

Next common occupation were students (18%), labourer (16%), Farmers (12%) and house wives (10%).

FIGURE 3: OCCUPATION



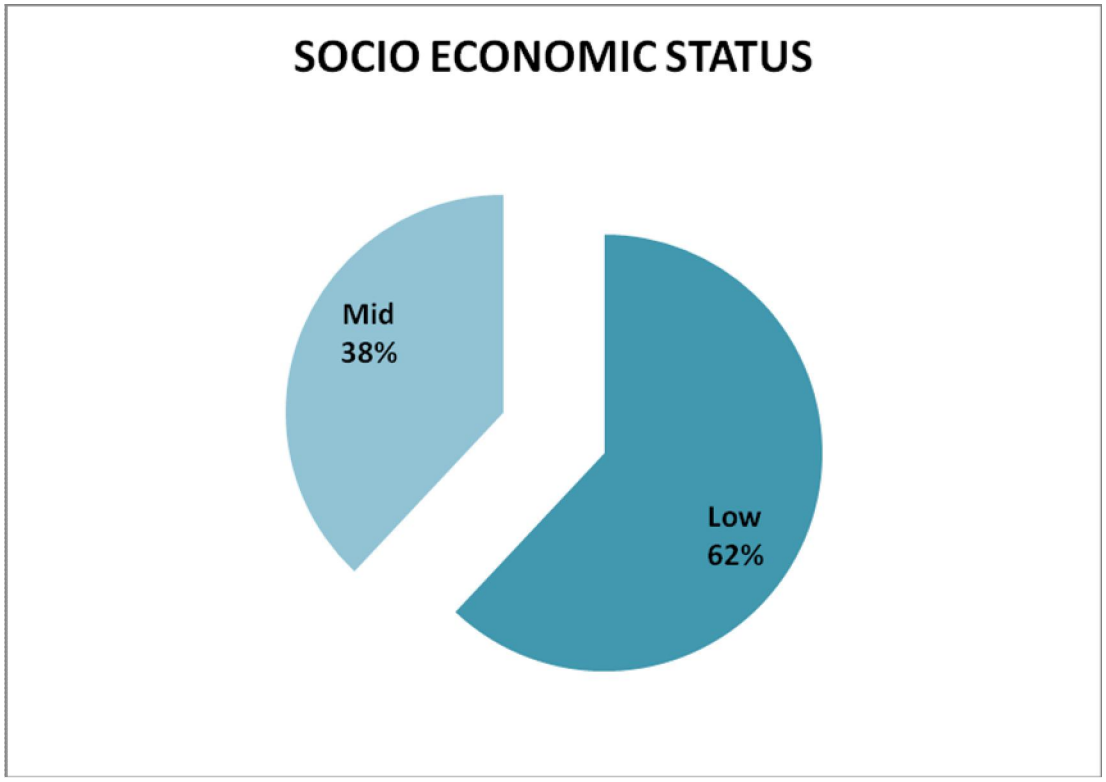
Socioeconomic status

In the present study, 62% were from Low income group whereas 38% patients were from Middle income group. There were no patients from High income group.

TABLE 5: SOCIOECONOMIC STATUS

SES	Frequency	Percent
Low	31	62.0
Mid	19	38.0
Total	**50**	**100.0**

FIGURE 4: SOCIOECONOMIC STATUS



Duration

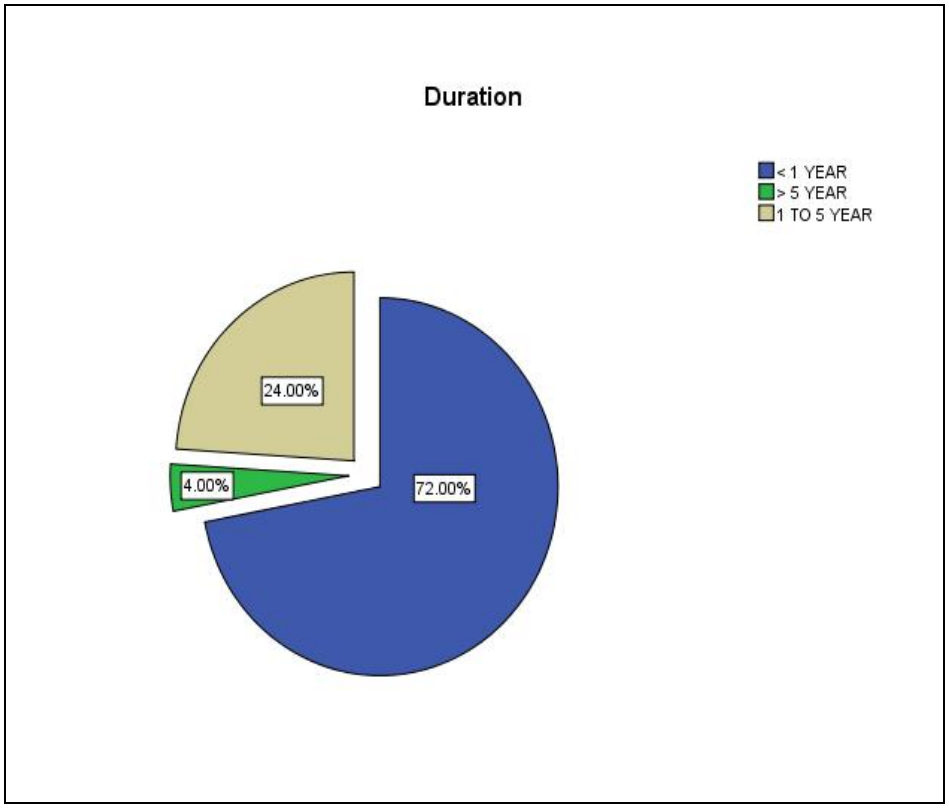
Minimum duration of disease was 1 month and maximum was 10 years.

- Maximum number of patients 36 i.e., 72% in this study had the disease duration of less than 1 year
- Duration was between 1-5 years in 12(24%)
- More than 5 years in 2(4%).

TABLE 6: DURATION

Duration	Frequency	Percent
< 1 YEAR	36	72.0
> 5 YEAR	2	4.0
1 TO 5 YEAR	12	24.0

FIGURE 5: DURATION



Complaints

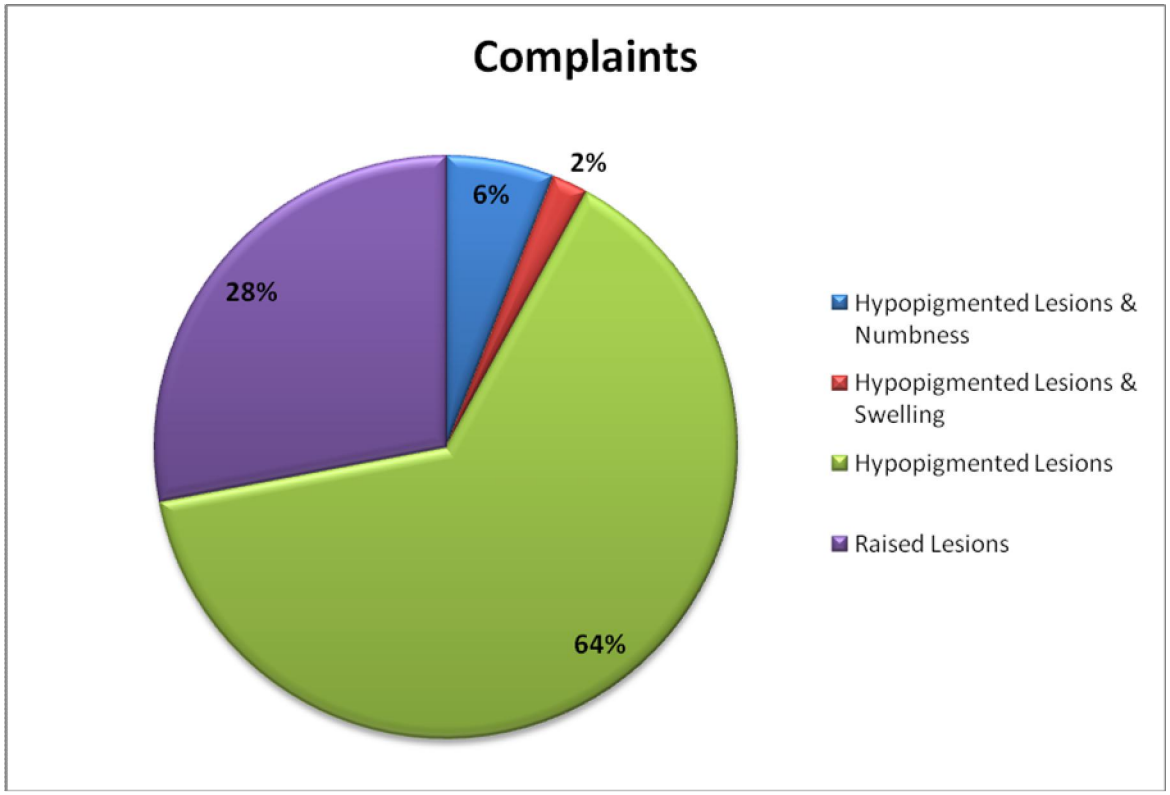
In this study out of 50 patients, 32(64%) patients had the complaints of hypopigmented skin lesion.

14(28%) patients had raised lesions. Numbness & hypopigmented lesions in 3(6%) patients and swelling & hypopigmented lesions in 1(2%) patients.

TABLE 7: COMPLAINTS

COMPLAINTS	Frequency	Percent
Hypopigmented lesions & Numbness	3	6.0
Hypopigmented lesions& swelling	1	2.0
Hypopigmented lesions	32	64.0
Raised lesions	14	28.0
Total	**50**	**100.0**

FIGURE 6: COMPLAINTS



Morphology

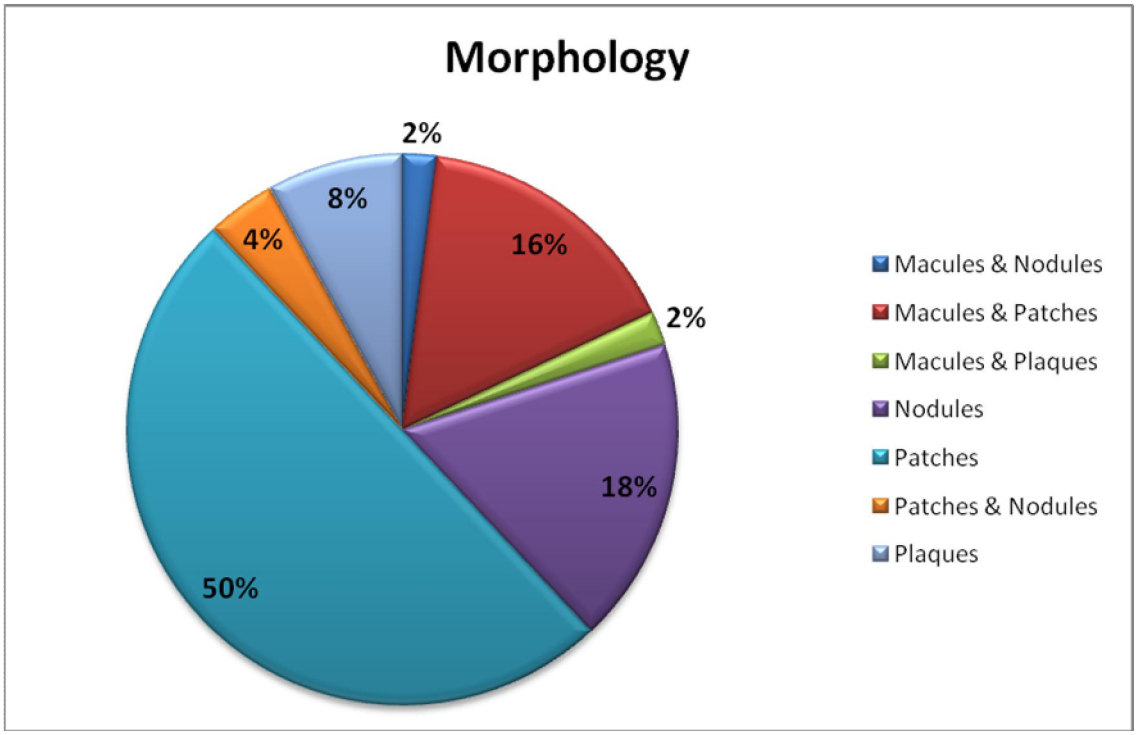
In this study majority of patients had patches on examination (50%). 18% of patients had nodules only.

16% had macules and patches, 8% had plaques, 4% had patches and nodules, 2% had macules & plaques and 2% had macules & nodules.

TABLE 8: MORPHOLOGY

Morphology	Frequency	Percent
Macules & Nodules	1	2.0
Macules & Patches	8	16.0
Macules & Plaques	1	2.0
Nodules	9	18.0
Patches	25	50.0
Patches & Nodules	2	4.0
Plaques	4	8.0
Total	**50**	**100.0**

FIGURE 7: MORPHOLOGY



Site distribution of skin lesions

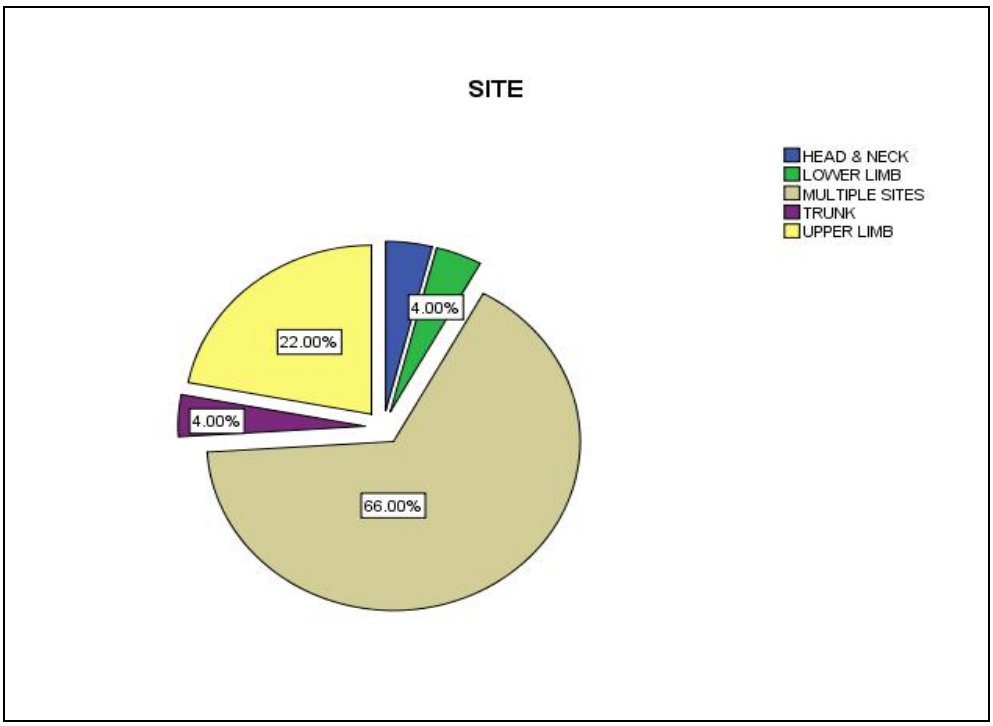
In our study among 50 patients, majority of patients had lesions over multiple sites of body.

- 33(66%) patients had lesions over multiple sites of body
- 11(22%) cases had lesions on upper limbs
- 2(4%) on the lower limb
- 2(4%) on trunk
- 2(4%) on the head & neck.

TABLE 8: SITE DISTRIBUTION

Site	Frequency	Percent
HEAD & NECK	2	4.0
LOWER LIMB	2	4.0
MULTIPLE SITES	33	66.0
TRUNK	2	4.0
UPPER LIMB	11	22.0
Total	**50**	**100.0**

FIGURE 7: SITE DISTRIBUTION



Clinical diagnosis

In our study all the patients were thoroughly examined clinically and diagnosed.

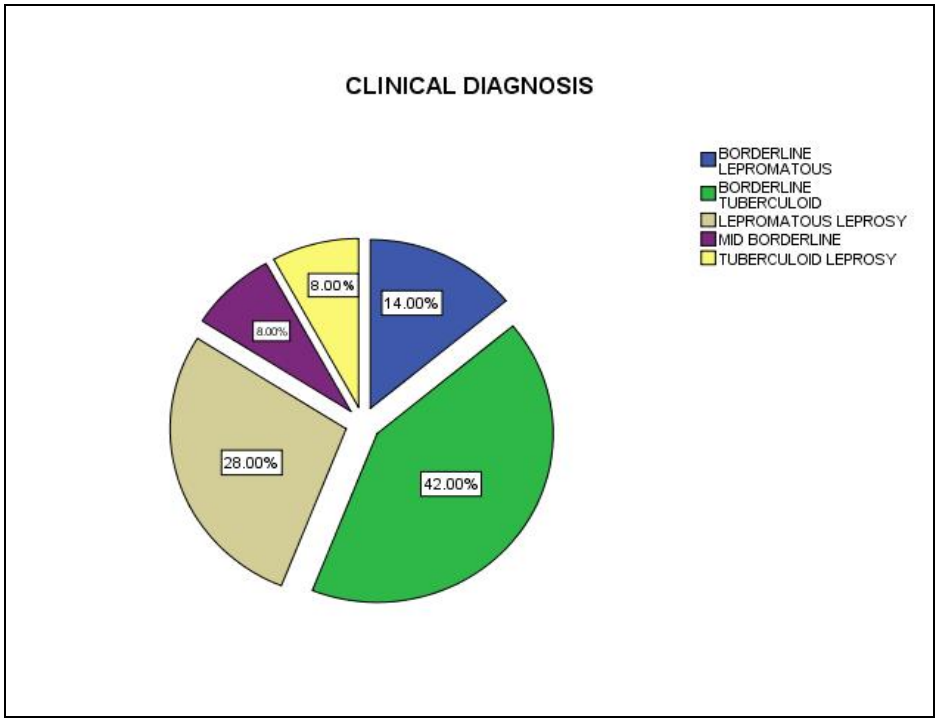
Out of 50 cases,

- 4(12%) were diagnosed as TT
- 21(42%) as BT
- 4(8%) as BB
- 7(14%) as BL
- 14(28%) as LL

TABLE 9: CLINICAL DIAGNOSIS

Clinical diagnosis	Frequency	Percentage
Tuberculoid leprosy	4	8.0
Borderline tuberculoid	21	42.0
Mid borderline	4	8.0
Borderline lepromatous	7	14.0
Lepromatous leprosy	14	28.0
Total	**50**	**100.0**

FIGURE 8: CLINICAL DIAGNOSIS



Slit skin smear-Acid fast bacilli

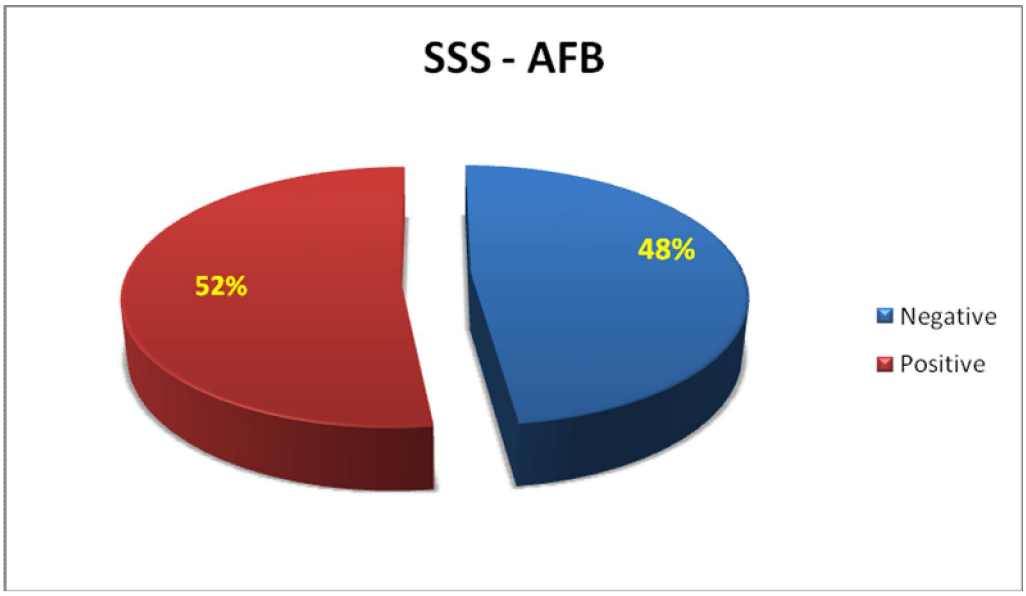
In our study 26(52%) patients showed smear positivity whereas 24(48%) showed smear negativity.

1(3.8%) BT patient, 4(15.4%) BB, 7(26.9%) BL and 14(53.8%) LL patient showed smear positivity. All tuberculoid patients were smear negative.

TABLE 10: SLIT SKIN SMEAR – AFB

SSS-AFB	Frequency	Percentage
NEGATIVE	24	48.0
POSITIVE	26	52.0
Total	**50**	**100.0**

FIGURE 9 : SLIT SKIN SMEAR- AFB



In this study 10% of smear positive patients had BI less than 3+ and 42% of patients had more than 3+ of BI.

TABLE 11: SSS- BI

BACTERIAL INDEX	Frequency	Percentage
<3+	5	10.0
>3+	21	42.0
Negative	24	48.0

FIGURE 10: SSS-BI

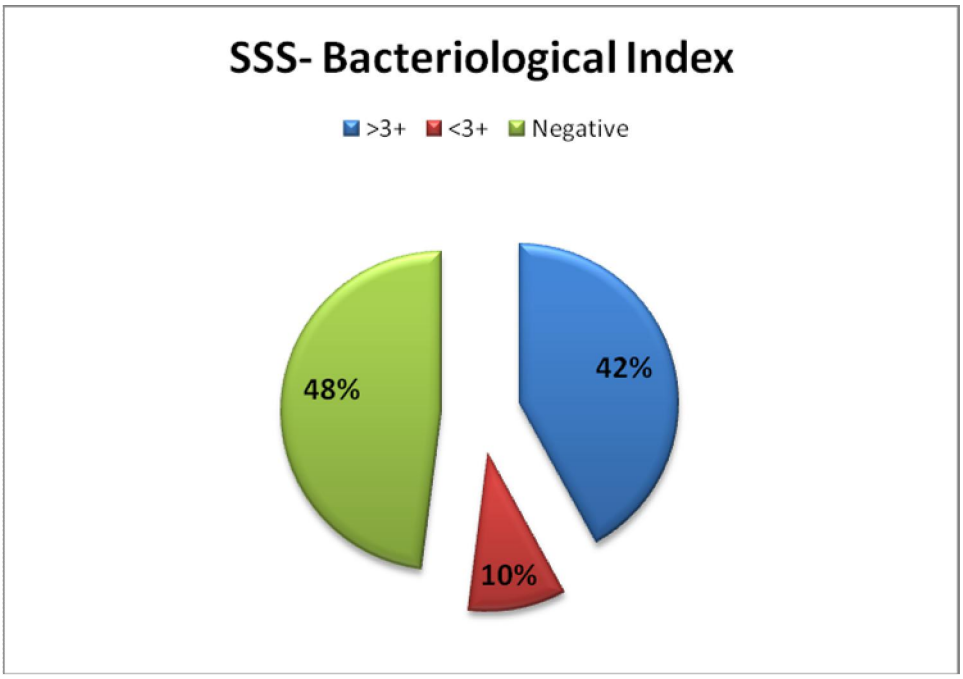
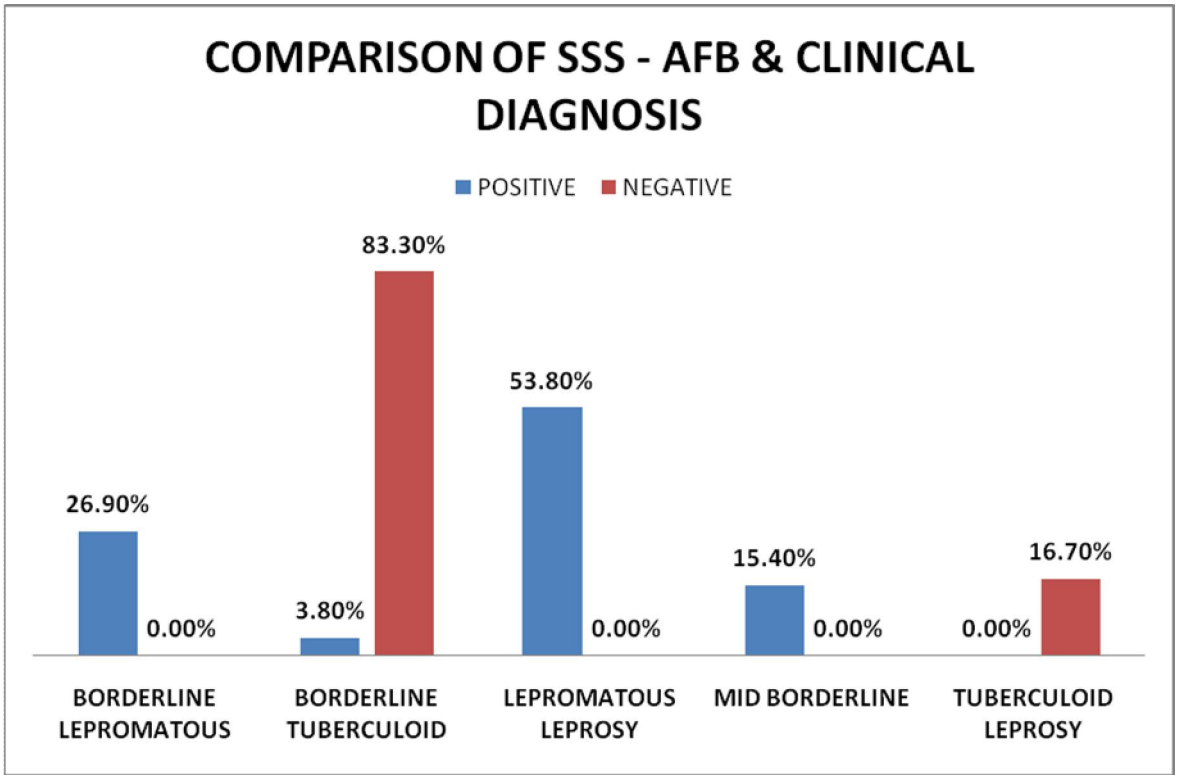


TABLE 12: SSS-AFB AND CLINICAL DIAGNOSIS

	CLINICAL DIAGNOSIS					
SSS - BI	**TUBERCULOID LEPROSY**	**BORDERLINE TUBERCULOID**	**MID BORDERLINE**	**BORDERLINE LEPROMATOUS**	**LEPROMATOUS LEPROSY**	**TOTAL**
POSITIVE	0	1	4	7	14	26
	0%	3.8%	15.4%	26.9%	53.8%	100.0%
NEGATIVE	4	20	0	0	0	24
	16.7%	83.3%	0%	0%	0%	100.0%
Total	4	21	4	7	14	50
	8.0%	42.0%	8.0%	14.0%	28.0%	100.0%

FIGURE 11 : COMPARISON OF SSS-AFB & CLINICAL DIAGNOSIS



Histopathological distribution

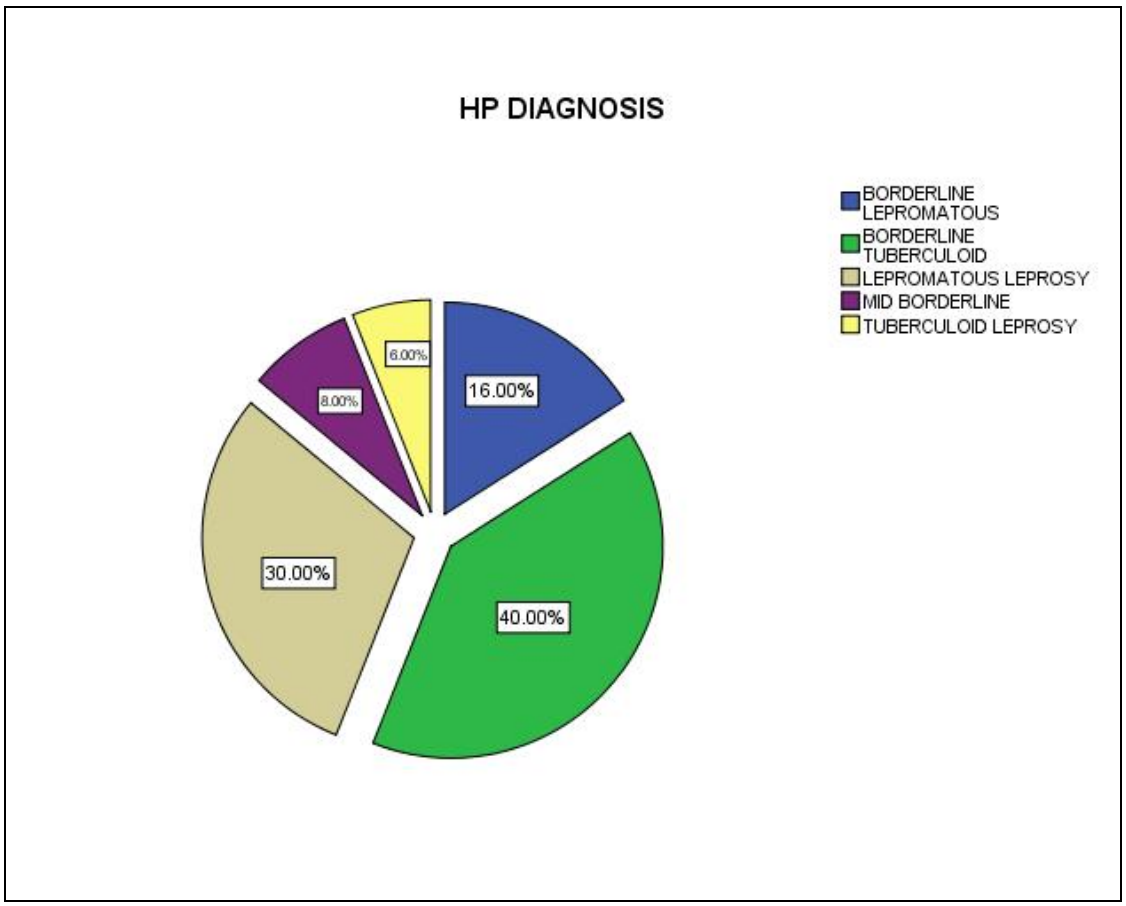
In our study skin biopsy was taken from all the 50 patients and stained with H & E stain.

- Out of 50 patients 20(40%) patients were histologically diagnosed as BT
- 15(30%) as LL
- 8(16%) as BL
- 4(8%) as BB
- 3(6%) as TT.

TABLE 13: HISTOPATHOLOGICAL DISTRIBUTION

Histopathological diagnosis	Frequency	Percent
TUBERCULOID LEPROSY	3	6.0
BORDERLINE TUBERCULOID	20	40.0
MID BORDERLINE	4	8.0
BORDERLINE LEPROMATOUS	8	16.0
LEPROMATOUS LEPROSY	15	30.0
Total	**50**	**100.0**

FIGURE 12 : HISTOPATHOLOGICAL DISTRIBUTION



Fite- Faraco stain

TABLE 14: FITE-FARACO STAIN

Fite-Faraco stain	Frequency	Percentage
NEGATIVE	30	60.0
POSITIVE	20	40.0
Total	**50**	**100.0**

Out of 50 patients, 20(40%) cases showed stain positivity and 30(60%) cases showed stain negativity. 5(25%) of BL and 15(75%) of LL patients showed stain positivity. Other types were negative.

TABLE 15: FITE-FARACO STAIN & HISTOPATHOLOGICAL DIAGNOSIS

Fite-faraco stain	Histopathological diagnosis					Total
	Tuberculoid leprosy	Borderline tuberculoid	Mid borderline	Borderline lepromatous	Lepromatous leprosy	
Positive	0 0%	0 0%	0 0%	5 25.0%	15 75.0%	20 100.0%
Negative	3 10.0%	20 66.7%	4 13.3%	3 10.0%	0 0%	30 100.0%
Total	8 16.0%	20 40.0%	15 30.0%	4 8.0%	3 6.0%	50 100.0%

FIGURE 13 :FITE-FARACO STAIN

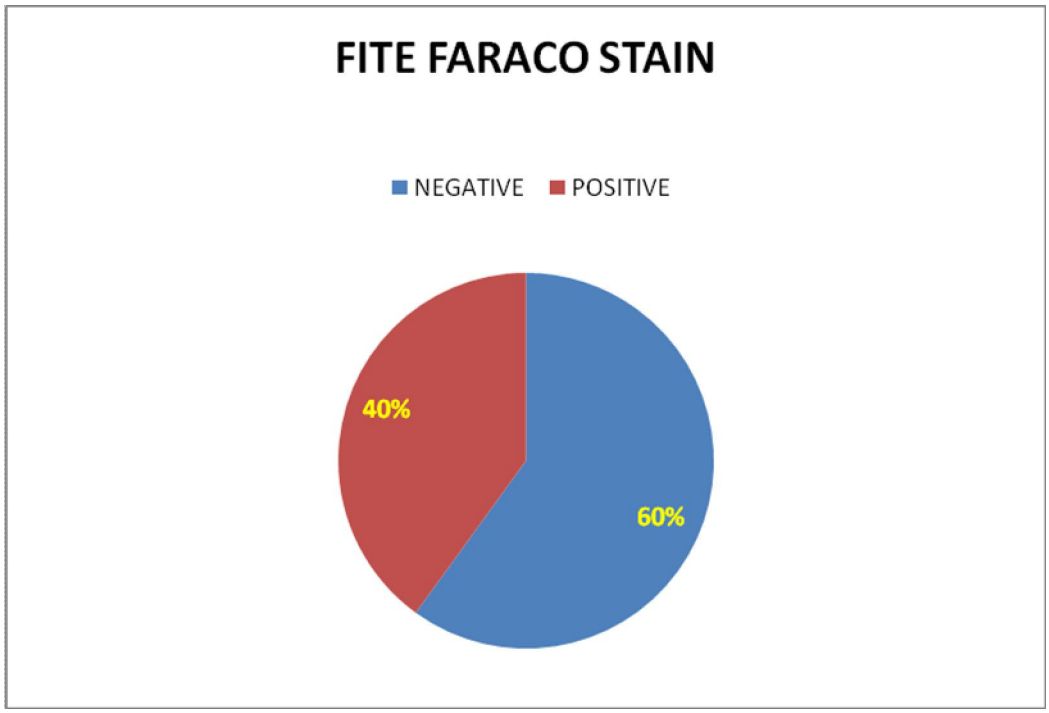
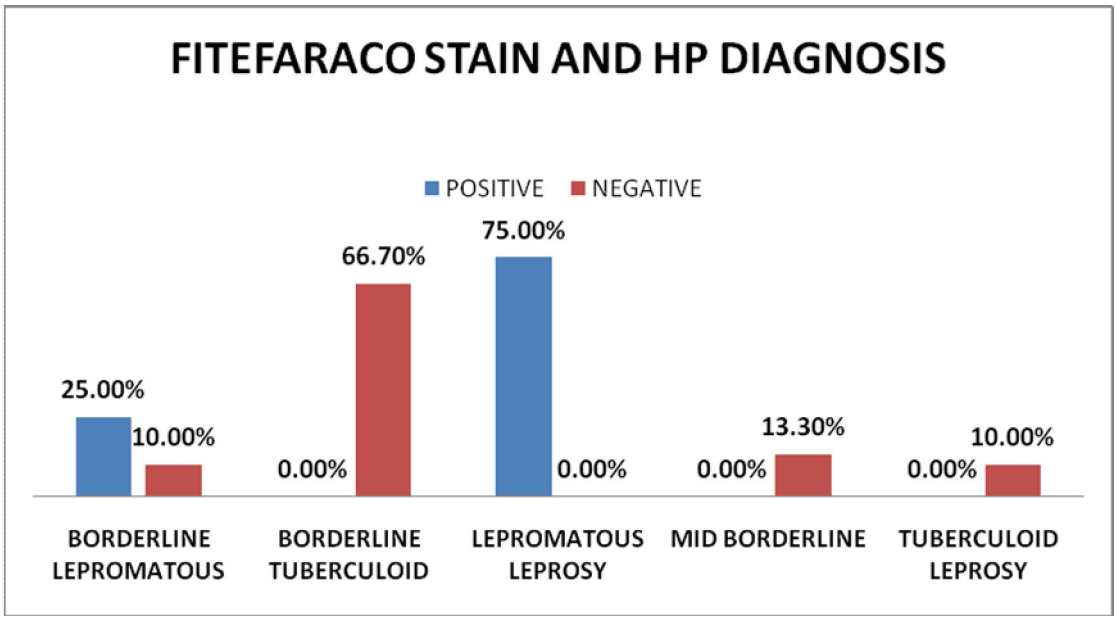


FIGURE 14: FITE-FARACO STAIN & HISTOPATHOLOGICAL DIAGNOSIS



Comparison of clinical and Histopathological diagnosis

TABLE 16: COMPARISON OF CLINICAL & HISTOPATHOLOGICAL DIAGNOSIS

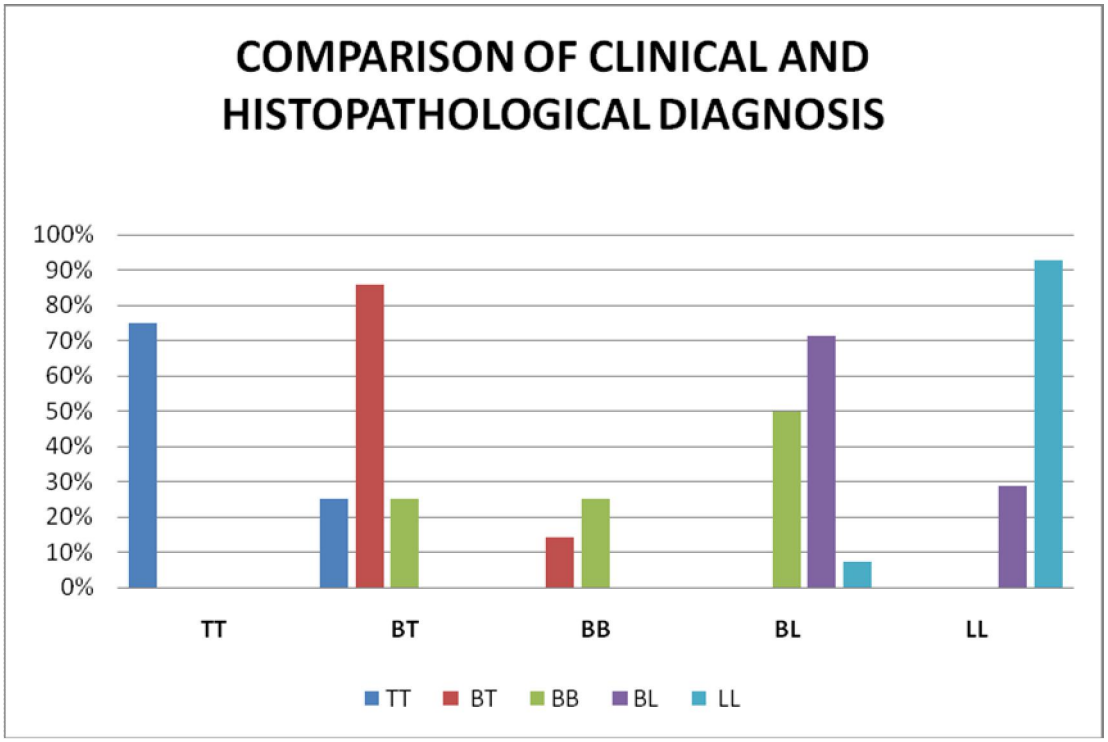
CLINICAL DIAGNOSIS	HISTOPATHOLOGICAL DIAGNOSIS				
	TT	BT	BB	BL	LL
TT (4)	**75% (3)**	**25% (1)**	**0% (0)**	**0% (0)**	**0% (0)**
BT (21)	**0% (0)**	**85.7% (18)**	**14.3% (3)**	**0% (0)**	**0% (0)**
BB (4)	**0% (0)**	**25% (1)**	**25% (1)**	**50% (2)**	**0% (0)**
BL (7)	**0% (0)**	**0% (0)**	**0% (0)**	**71.4% (5)**	**28.6% (2)**
LL (14)	**0% (0)**	**0% (0)**	**0% (0)**	**7.1% (1)**	**92.9% (13)**

Clinico-histopathological agreement was seen in 40 (80%) cases and disagreement in 10 (20%) cases.

Out of 4 patients clinically diagnosed as TT, 3(75%) patients had histopathological correlation. Out of 21 patients clinically diagnosed as BT, 18(85.7%) patients had histopathological correlation.Out of 4 patients clinically diagnosed as BB only one patient had histological correlation, out of 7patients clinically diagnosed as BL, 5 patients had histopathological correlation, out of 14 patients clinically diagnosed as LL, 13 patients had histopathological correlation.

FIGURE 15: COMPARISON OF CLINICAL &

HISTOPATHOLOGICAL DIAGNOSIS



DISCUSSION

In the present study, Ridley-Jopling classification was used to classify leprosy histopathologically in all cases. Indeterminate leprosy was not included for analysis. Histoid leprosy is considered as a variant of Lepromatous leprosy and it was included in LL spectrum.

Age distribution

In the present study more number of patients belong to the age group of 21-40 years(52%).

In a study done by Moorthy BN et al [85], majority of patients were between 20-29 years (20.70%).

Singh et al [86], found the disease in 48% of patients belonging to age group of 21- 40 years.

Santaram and Porichha[87] found majority of patients were 21- 40 years.

Similarly Jindal et al[88] and Samuel et al[89] found the disease in 48% of patients belonging to the age group of 21- 40 years.

Thus the age incidence in the present study correlates well with the other studies. The disease is more common in this age group because of their mobility and increased opportunity for contacts.

Sex distribution

In the present study 82% of patients were males and 18% were females. Similarly Santaram and Porichaa found the disease in 80% of males.

Singh et al[86] found the disease in 69% of males.

Similarly Moorthy et al[85], Gridhar M et al [90] and Nitesh Mohan et al [91] found the disease to be more common in males.

Comparison of sex in various studies

Authors	-	**Males (%)**
Santaram et al [87]	-	80
Singh et al [86]	-	69
Moorthy et al [85]	-	65.05
Bhushan et al [92]	-	72.34
Mathur MC et al [93]	-	53.8
Gridhar M et al [90]	-	77.6
Nitesh Mohan et al[91]	-	72.10
Present study	-	82

The result of the present study is close to the above mentioned studies with regard to the sex. This disease is more common in males because of their outdoor works and higher chances of getting infection.

Occupation

In the present study majority of patients were coolies(42%).

Next common occupation were students (18%), labourers (16%), Farmers (12%) and house wives(10%).

Similar observation was noted in the study by Ramanjanayalu[94]. In that 41% of patients were coolies.

Choudhuri et al [94] 90% of patients were agricultural workers. Thappa et al[95] found manual labourers comprised 53.9% of patients.

This is due to low economic status among people in manual work.

Socioeconomic status

In the present study 62% of patients were from low income group and 38% of patients were from middle income group.

Similar observations were made by Mutakar[97] and Chhabriya et al[98] , the majority of patients belonged to low income group.

Singh et al[86] found the disease in 57% of patients belonging to low socioeconomic status.

Thus the disease is common in people from low socioeconomic status. This is because of the fact that low income group is always associated with illiteracy, over crowding, malnutrition and lack of personal hygiene, which are the important factors in acquisition of the disease in case of leprosy.

Duration

The duration of illness in the present study was less than 1 year in 72% of patients, 1-5 years in 24% and more than 5 years in 4% of patients.

Similarly Ramanjanayalu [94] found the duration of illness was less than 6 months in 54% of patients, 1-5 years in 24% and 6-11 months in 17% of patients.

Wim et al[99] , found the duration was up to 6 months in 30% of patients, 7-12 months in 32%, 13-24 months in 17%, 25-36 in 9.3%, 37-60 months in 6.3% and more than 60 months in 5.4%.

Thus most of the patients had the illness for the duration of less than 1 year. This is because of the patients present to the hospital earlier.

Complaints

In this study out of 50 patients, 32(64%) patients had the complaints of Hypopigmented skin lesion.

14(28%) patients had Raised lesions, Numbness & Hypopigmented lesions in 3(6%) patients and swelling & hypopigmented lesions in 1(2%) patients.

Similarly Nitesh Mohan et al[91] found that most common clinical presentation was hypopigmented patch (61.58%) followed by erythematous plaque or nodule (38.42%). This also correlated well with study done by M Gridhar et al[90] and Ocampo and Francisco.

Hypopigmented anesthetic skin lesion is one of the cardinal sign of leprosy.

Morphology

In this study majority of patients had patches on examination (50%) . 18% of patients had nodules only.

16% had macules and patches, 8% had plaques, 4% had patches and nodules, 2% had macules & plaques and 2% had macules & nodules.

There are no many available studies to compare this parameter.

Site of lesion

In the present study 66% of patients had the lesions over multiple body sites and 22% had the lesions on upper limbs.

But in the study done by Nitesh Mohan et al[91] , 34.21% of patients had the lesion on upper limbs, 21.05% of patients had on head& neck site and 15.79% on multiple sites.

There are no many available studies to compare this parameter.

Clinical diagnosis

In the present study, out of 50 patients , 42% were diagnosed as BT, 28% as LL, 14% as BL, 8% as TT and 8% as BB.

Nitesh Mohan et al [91] found BT in 45.26%, LL in 23.68%, BL in 13.68%, TT in 7.89% and BB in 2.12% of patients.

Similarly Ramanjanayalu[94] and Zhongdong [100] found that majority of patients had BT.

Jindal et al[88] found LL in 33%, BT in 28%, BL in 23%, TT in 5.5% and BB in 4% of patients.

Vara and Marfatiya[101] found BT in 36%, LL in 52%, TT in 13%, BB in 9% and BL and pure neuritic in 8%.

Thus the results in the present study correlate well with other studies and most common clinical type was Borderline tuberculoid.

SSS-Acid fast bacilli

In the present study 52% of patients showed smear positivity and 48% of patients showed smear negativity.

Smear positivity was less than 3+ in 10% of patients and more than 3+ in 42% of patients.

All BB, BL and LL patients were smear positive and all TT patients were smear negative. 3.8% of BT patients only smear positive.

Ramanjanayalu[94] found overall positivity in 39% of patients and negativity in 60% of patients.

Vara and Marfatiya[101] found positivity in 38% of patients.

In the study of Vara[102], smear positivity was less than 3+ in 28% of patients and more than 3+ in 18% of patients. Smear negativity in 54% of patients.

The smear positivity in the present study is more than above mentioned studies. This is probably because of clinical typing of patients.

Histopathological distribution

In our study 40% of patients histopathologically diagnosed as BT patients, 30% as LL, 16% as BL, 8% as BB and 6% as TT.

Similarly Nitesh Mohan et al[91] found 44.4% as BT, 19.05% as LL, 14.8% as IL, 12.7% as BL, 7.4% as TT and 1.6% as BB.

In the study of Manandhar et al[103] , 40% of patients histopathologically diagnosed as BT.

Thus histologically, the common classification made was Borderline tuberculoid.

Fite-Faraco stain

Fite-Faraco stain was positive in 40% of patients and negative in 60% of patients.

In that positive patients, 75% were belonging to LL and 25% were belonging to BL.

Manandhar et al[103] found positive in 25% of patients. In contrast to our study, various studies reported better demonstration of AFB in biopsy than in slit skin smear.

Bhusan P et al[92] . found significant number of positive cases in biopsy which constituted 65 (46.09%) cases while SSS positive only in 43 (30.05%) cases.

AFB are better demonstrated usually in biopsies than in slit skin smear due to presence of AFB in deep reticular dermis where they remain inaccessible to SSS.

Clinico-histopathological correlation

In our study skin biopsy was done in all 50 patients.

Clinico-histopathological agreement was seen in 40 (80%) cases and disagreement in 10 (20%) cases.

Out of 4 patients clinically diagnosed as TT, 3(75%) patients had histopathological correlation.

Out of 21 patients clinically diagnosed as BT, 18(85.7%) patients had histopathological correlation.

Out of 4 patients clinically diagnosed as BB only one(25%) patient had histological correlation.

Out of 7 patients clinically diagnosed as BL, 5(71.4%) patients had histopathological correlation.

Out of 14 patients clinically diagnosed as LL, 13(92.9%) patients had histopathological correlation. There was complete agreement between the clinical and histopathologic diagnosis in 80% of the cases.

Comparative study in clinico-pathological correlation by different authors.

Various studies	-	**Clinicohistopathological correlation(%)**
Manandhar et al[103]	-	45.33
Nitesh Mohan et al[91]	-	5.54
Sehgal VN et al[104]	-	33
Vargas-ocampo F et al [105]	-	42.9
Mitra K et al[106]	-	57.16
Pandya AN et al[107]	-	58
Moorthy BN et al[85]	-	62.63
Kalla G et al[108]	-	64.7
Ridley DS et al[109]	-	68.3
Jerath VP et al[110]	-	68.5
Bhatia AS et al[111]	-	69
Kar PK et al[112]	-	70
Nadkarni NS et al[113]	-	81.8

In the present study, Maximum concordance was observed in LL type of leprosy, which was similar in studies by Mathur MC et al[93], Gridhar M et al[90] and Moorthy et al.

TABLE 17: CLINICO-PATHOLOGICAL CORRELATION IN VARIOUS SPECTRUM IN VARIOUS STUDIES

Types of leprosy	Mohan et al	Manandhar et al	Moorthy BN et al	Nadkarni NS et al	Kar et al	Kalla et al	Jerath& Desai	Present study
TT	71.93	24	46.15	97	87.5	75.6	74.5	75
BT	79.76	63.15	66.66	95	60.9	44.2	64.7	85.7
BB	66.67	0	50	89	54.5	37	28.5	25
BL	66.67	57.14	70	87	53.8	43.7	53.8	71.4
LL	97.22	57.14	80	98	71.4	76.7	61.5	92.9
IL	50	0	20	-	81.2	-	88.8	-

Different studies observed highest percentage of clinicopathological correlation of lepromatous leprosy and tuberculoid leprosy in their studies and showed least clinic-pathological correlation in midboderline lepomatous leprosy.

In contrast to our study, Nayak SV et al[114] study showed maximum correlation in midborderline (100%).

Ridley and Jopling found complete agreement between clinical and histopathological types in 68.3%[37].

There was a minor disagreement (disagreement in one group) in 10 (20%) cases and no major disagreement (more than one group). Ridley and Jopling, found minor disagreement in 21 patient (25.6%), major disagreement in 5 patient (6%).

The variation in different studies may be due to different criteria used to select the cases and difference in number of cases of each type. Various factors also influence the histopathological diagnosis such as differences in sample size, choosing the biopsy site, age of the lesion, immunological status of the patient at the time of biopsy.

SUMMARY

- Majority of patients (52%) belongs to the age group of 21- 40 years.
- Male patients comprised 82% and female patients were 18%.
- Majority of patients were coolies (42%). Next common occupation were students (18%), labourers (16%), Farmers (12%) and house wives (10%).
- 62% of patients were from Low socioeconomic group and 38% of patients from Middle income group.
- 72% of patients had the disease duration of less than 1 year, 24% had the duration between 1-5 years and more than 5 years in 4% of patients.
- 32(64%) patients had the complaints of Hypopigmented skin lesion. 14(28%) patients had Raised lesions, Numbness & Hypopigmented lesions in 3(6%) patients and swelling & hypopigmented lesions in 1(2%) patients
- Majority of patients had patches on examination (50%) , 18% of patients had nodules only.

- 66% patients had the lesions over multiple sites of the body, 22% cases had the lesion on upper limb, 4% on the lower limb, 4% on the trunk and 4% on the head & neck.
- Borderline tuberculoid was the most common clinical presentation comprising of 42%.
- 52% of patients showed Acid fast stain positivity and 48% were smear negative. 1(3.8%) BT patient, 4(15.4%) BB, 7(26.9%) BL and 14(53.8%) LL patients showed smear positivity.
- Out of 50 patients 40% patients were histologically diagnosed as BT, 30% as LL, 16% as BL, 8% as BB and 6% as TT.
- 40% of patients showed Fite-Faraco stain positivity in biopsy specimen. 5(25%) of BL and 15(75%) of LL patients showed stain positivity.
- Clinico-histopathological agreement was seen in 80% of cases and disagreement was seen in 20% of cases.

Out of 4 patients clinically diagnosed as TT, 3(75%) patients had histopathological correlation. Out of 21 patients clinically diagnosed as BT, 18(85.7%) patients had correlation. 25% of BB patients had clinichistopathological correlation, 71.4% of BL and 92.9% of LL patients had clinicohistopathological correlation.

CONCLUSION

In our study,

- The higher incidence in the age group 21-40 years is because of their mobility and increased contact with the infective persons.
- The incidence was higher in males because of their more physical activity and thus more chances of getting infection. Because of ignorance and hesitation to come forward to treatment, low incidence is seen in females.
- Majority of patients were coolies.
- Most of the people affected were from low socioeconomic group.
- The duration of illness was less than one year in majority of patients.
- Most common complaint was hypopigmented skin lesions.
- The higher number of patients were Borderline tuberculoid. This is because, these patients come early for the treatment because of its neurological symptoms.
- SSS-AFB positivity was found in 52% of patients but Fite-Faraco stain of skin biopsy showed positivity in 40% of cases.

- ❖ Clinico-histopathological correlation was seen in 80% of the patients. Maximum correlation was observed in Lepromatous leprosy. So, LL patients can be diagnosed clinically.

In conclusion it can be said Leprosy still continues to be a domestic, national, global burden and is present in different clinico-pathological forms.

Many cases can be diagnosed clinically; especially Lepromatous pole of the disease, however, other types of Leprosy pose a significant problem in clinical diagnosis. Histopathological examination of the lesions confirms the exact subtype of the disease and facilitate the institution of accurate mode of therapy. So, correlation of clinical and histopathological features along with bacteriological index is more useful for accurate typing of leprosy than considering single parameter alone.

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PROFORMA

NAME :

AGE/SEX :

OP/IP No :

ENROLLMENT No :

PHONE :

ADDRESS :

OCCUPATION :

INCOME :

EDUCATION STATUS :

SOCIOECONOMIC STATUS:

Chief complaints with duration of illness:

H/o Presenting illness:

Onset:

Progression:

	Present	Absent
Hypopigmented skin lesion		
Loss of sensation over lesion		
Loss of sweating/loss of hair		
Pain/itching over lesion		
Nasal stuffiness/epistaxis		
Pedal edem		
Fever/joint pain		
Watering of eyes/photophobia		
Glove & Stocking anaesthesia		
Difficulty in combing hair		
Difficulty in holding chappals		
Hand/Foot deformity		
Any new drug intake		
Increase in size/number of lesions		

PAST HISTORY:

Co-morbid medical illness:

If so what :

FAMILY HISTORY :

CONTACT HISTORY :

EXPOSURE HISTORY :

GENERAL EXAMINATION :

Face: nodules/skin thickening/Madarosis/Corneal ulceration

Nasal deformity:

Ear lobe infiltration:

Gynaecomastia

Testicular atrophy:

DERMATOLOGICAL EXAMINATION:

Skin lesion:

Number

Site

Size

Symmetry

Edges

Borders

Surface : smooth / dry / scaly / erythematous / necrosis

Induration

Sensation

Loss of hair

Loss of sweating

Satellite lesions

Nerve twigs

Sensory system: Pain &Temperature

Peripheral nerves:

Nerve	**Right**		**Left**	
	Thickening	**Tenderness**	**Thickening**	**Tenderness**
Supra-orbital N.				
Infra-orbital N.				
Greater Auricular N.				
Clavicular Ns.				
Ulnar N.				
Median N.				
Radial cutaneous N.				

Lateral Popliteal N.				
Sural N.				
Posterior Tibial N.				
Anterior Tibial N.				

Motor System: UL LL

Power/Movements

Weakness/Deformity

Trophic ulcers/Resorption of digits

CLINICAL DIAGNOSIS:

Investigations:

CBC:

BT / CT:

VCTC:

SSS:

Skin Biopsy:

Haematoxylin & Eosin stain:

Modified Fite Faraco stain:

HISTOPATHOLOGICAL DIAGNOSIS:

ABBREVIATIONS

SES	-	Sosioeconomic status
Hypo. P	-	Hypopigmented lesions
M. leprae	-	Mycobacterium leprae
TT	-	Tuberculoid
BT	-	Borderline tuberculoid
BB	-	Mid borderline
BL	-	Borderline lepromatous
LL	-	Lepromatous
R. elbow	-	Right elbow
R. arm	-	Right arm
R. forearm	-	Right forearm
R. shoulder	-	Right shoulder
R. thigh	-	Right thigh
R. leg	-	Right leg
L. Shoulder	-	Left shoulder
L. arm	-	Left arm
L. forearm	-	Left forearm
L. thigh	-	Left thigh
L. leg	-	Left leg

B. arms	-	Both arms
B. forearms	-	Both forearms
B. thighs	-	Both thighs
B. legs	-	Both legs
G & S	-	Glove & stocking anesthesia
Y	-	Yes
R. UL	-	Right ulnar nerve
L.UL	-	Left ulnar nerve
B. UL	-	Both ulnar nerves
R.RC	-	Right radial cutaneous
L. RC	-	Left radial cutaneous
B. RC	-	Both radial cutaneous
R. GA	-	Right greater auricular
L. GA	-	Left greater auricular
B. GA	-	Both greater auricular
R. LP	-	Right lateral popliteal
L. LP	-	Left lateral popliteal
B. LP	-	Both lateral popliteal
B. SN	-	Both sural nerve
SSS	-	Slit skin smear
BI	-	Bacteriological Index

Hp	-	Histopathology
P	-	Positive
N	-	Negative

PATIENT CONSENT FORM

Title of the study : Clinico-Histopathological correlation in various spectrum of Leprosy

Name of the Participant :

Name of the Principal Investigator : Dr. B. AMALA

Name of the Institution : Department of Dermatology & Leprosy,

Rajiv Gandhi Government General Hospital,

Chennai

Documentation of the Informed Consent : (legal representative can sign if the participant is minor or incompetent)

I _____ have read/it has been read for me, the information in this form. I was free to ask any questions and they have been answered. I am over 18 years of age and exercising my free power of choice, hereby give my consent to be included as a participant in the study.

1. I have read and understood this consent form and the information provided to me.
2. I have had the consent document explained in detail to me.
3. I have been explained about the nature of my study.
4. My rights and responsibilities have been explained to me by the investigator.
5. I agree to cooperate with the investigator and I will inform her immediately if I suffer from unusual symptoms.
6. I have not participated in any research study at any time.
7. I am aware of the fact that I can opt out of the study at any time without having to give any reason and this will not affect my future treatment in this hospital.
8. I hereby give permission to the investigators to release the information obtained from me as a result of participation in this study to the regulatory authorities, government agencies, and

Institutional Ethics Committee. I understand that they are publicly presented.

9. My identity will be kept confidential if my data are publicly presented.
10. I am aware that if I have any question during this study, I should contact the concerned investigator

Participant's Initials : _____

Name and signature/thumb impression of the participant (or legal representative if participant is minor or incompetent)

_____ _____ _____

Name Signature Date

Name and signature of impartial witness (required for illiterate patients)

_____ _____ _____

Name Signature Date

Address and contact number of the impartial witness :

Name and signature of the investigator or his representative obtaining consent:

_____ _____ _____

Name Signature Date

INTRODUCTION

Leprosy, also known as Hansen's disease, is one of the oldest disease of mankind. Leprosy still remains an important public health problem in MANY parts of Asia, MAINLY India.

In our country despite declaring leprosy elimination at national level in January 2006 it is still a disease of endemic in many states. The total estimated global new cases detected in 2009 were 2, 27, 849 and India account 1,33,717 (58.7%) cases.

Depending on the immune status of the host, Leprosy presents in various clinico-pathological forms. Leprosy can be diagnosed by various methods including detailed clinical examination of the skin lesions and peripheral nerves, demonstration of the Acid Fast Bacilli (AFB) in slit skin smears by Ziehl-Nielsen staining, Histopathological section, demonstration of bacilli by modified Fite Faraco procedure[10], and Fine Needle Aspiration Cytology (FNAC) of nerves.

Ridley and Jopling have suggested immunological basis of leprosy and classified into five types as Tuberculoid Leprosy (TT), Borderline tuberculoid Leprosy(BT), Mid-borderline Leprosy (BB), Borderline Lepromatous Leorosy (BL), and Lepromatous Leprosy (LL). This Classification is accepted worldwide and is highly recommended.

INSTITUTIONAL ETHICS COMMITTEE
MADRAS MEDICAL COLLEGE, CHENNAI -3

EC Reg. No. ECR/270/Inst./TN/2013
Telephone No. : 044 25305301
Fax : 044 25363970

CERTIFICATE OF APPROVAL

To
Dr.B. Amala,
PG in M.D. Dermatology, Venerology, Leprology
Department of Dermatology,
Madras Medical College, Chennai -3.

Dear Dr.B. Amala,

The Institutional Ethics Committee of Madras Medical College reviewed and discussed your application for approval of the proposal entitled **"CLINICO HISTOPATHOLOGICAL CORRELATION IN VARIOUS SPECTRUM OF LEPROSY"** No. 01112013

The following members of Ethics Committee were present in the meeting held on 13.11.2013 conducted at Madras Medical College, Chennai -3.

1. Dr. G. Sivakumar, MS FICS FAIS -- Chairperson
2. Prof. R. Nandini, MD -- Member Secretary
   Director, Instt.of Pharmacology, MMC, Ch-3
3. Prof. Ramadevi, MD -- Member
   Director i/c, Instt.of Biochemistry, MMC, Chennai.
4. Prof. P. Karkuzhali, MD -- Member
   Professor, Instt.of Pathology, MMC, Ch -3.
5. Prof. Kalai Selvi. MD -- Member
   Prof. of Pharmacology, MMC, Ch -3.
6. Thiru. S. Govindasamy, BA BL -- Lawyer
7. Tmt. Arnold Saulina, MA MSW -- Social Scientist

We approve the proposal to be conducted in its present form.

Sd/ Chairman & Other members

The Institutional Ethics Committee expects to be informed about the progress of the study, and SAE occurring in the course of the study, any changes in protocol and patients information / informed consent and asks to be provided a copy of the final report.

Member Secretary, Ethics Committee

MEMBER SECRETARY
INSTITUTIONAL ETHICS COMMITTEE
MADRAS MEDICAL COLLEGE
CHENNAI-600 003

S.NO.	Name	Age	Sex	Occupation	SES	Duration	Complaints	SKIN LESIONS																								PERIPHERAL NERVES		Trophic changes	Deformity	Clinical Diagnosis	SSS - BI	HP Diagnosis	Fite-Faraco stain
								Morphology	Number	Site	Size			Shape		Colour		Surface		Margin			Infiltration	Satellite lesion	Hair			Sensation			Sensory system	Thickening	Tenderness						
											Small	Big	Variable	Circular	Irregular	Erythematous	Hypo pig	Dry	Shiny	Well defined	Well - ill	Ill defined			Normal	Sparse	Absent	Normal	Impaired	Absent								
1	Dhandabani	56	Male	Farmer	Mid	1 mon	Hypo P	Patches	3	Back		Y		Y			Y	Y			Y				Y			Y			B.UL R.RC				BT	0	BT	N
2	Muthu krishnan	36	Male	Business	Mid	6 mon	Hypo P	Patches	2	R. elbow		Y		Y			Y	Y			Y			Y			Y				R.UL R.RC				BT	0	BT	N
3	Sujith	18	Male	Painter	Low	1Yr	Hypo P	Patches Macules	>20	B.arms Face Chest Legs			Y		Y		Y		Y			Y			Y				Y			R.GA B.UL R.RC B.LP				BL	4+	BL	P
4	Barathy mohan	29	Male	Farmer	Low	3mons	Hypo P	Patches	1	Lt.arm		Y		Y			Y	Y				Y		Y			Y				L.UL				BT	0	BT	N
5	Kuppammal	50	Female	House wife	Low	8 mons	Raised lesion	Nodules	>20	face arm forearm trunk buttock thigh			Y		Y						Y		Ear lobe		Y			Y			G & S	B.GA B.UL B.RC B.LP		R.feetUlcer		LL	6+	LL	P
6	Ramachandran	39	Male	Driver	Mid	6 mons	Hypo P	Patches	1	L.forearm		Y		Y			Y					Y		Y		Y					B.UL				BT	0	BT	N
7	Rajiv gandhi	21	Male	Student	Mid	2Yrs	Hypo. P	Patches	6	R. elbow Back		Y		Y			Y	Y			Y			Y			Y		Y		B.UL R.RC				BT	0	BT	N
8	Sathish	27	Male	Coolie	Low	1Yr	Hypo. P	Patches	3	L.shoulder L.forearm		Y		Y			Y	Y				Y		Y			Y				R.UL R.RC				BT	0	BT	N
9	Swaminathan	58	Male	Farmer	Mid	2 mon	Hypo. P	macules Patches	18	b.forearm Chest Back			Y		Y		Y	Y	Y			Y		Y					Y			B.UL B.RC R.LP	Y			BB	4+	BL	N
10	Rama moorthy	32	Male	Coolie	Low	3Yrs	Raised lesion Hypo. P	Nodules Plaques Patches	Multiple	B.arms B.forearms Chest Back B.legs	Y				Y		Y		Y				Ear lobe		Y					Y	G & S	R.GA B.UL B.RC B.LP				LL	5+	LL	P
11	Balaji	24	Male	Student	Low	2Yrs	Hypo. P Numbness	Patch	1	R. elbow		Y			Y		Y	Y				Y				Y			Y		B.UL R.RC				BT	0	BT	N
12	Karthick	9	Male	Student	Mid	6 mon	Hypo.P	Patch	1	R.forearm		Y		Y			Y	Y			Y			Y		Y			Y			R.UL R.RC	Y			BT	0	BT	N
13	Jaysor	32	Male	Coolie	Low	2 mon	Raised lesion	Nodules	Multiple	B.arms B.forearms Chest	Y					Y			Y						Y			Y				B.UL B.RC				LL	6+	LL	P
14	Sathyavanan	38	Male	Driver	Mid	1Yr	Raised lesions	Nodules	Multiple	Face B.arms B.forearms Chest B.thighs B,legs			Y										Face Ear lobe		Y					Y	G & S	B.GA B.UL B.LP			R. Claw hand	LL	5+	LL	P
15	Amirtham	50	Female	Coolie	Low	10Yrs	Loss of sensation Hypo. P	Patches	4	Back L.forearm		Y		Y			Y				Y			Y		Y			Y			L.UL L.RC				BT	0	BT	N
16	Rathna velu	36	Male	Business	Low	5Yrs	Hypo. P	Patches	5	Back L.thigh L.leg			Y	Y			Y	Y			Y			Y			Y			Y		B.UL B.LP				BT	0	BT	N
17	Paul raj	30	Male	Mechanic	Low	1Yr	Raised lesion	Nodules	Multiple	Chest back Abdomen B.arms B.forearms B.legs			Y			Y			Y						Y			Y				R.UL R.RC				LL	4+	BL	P

18	Sujatha	30	Female	Labourerer	Low	1Yr	Hypo. P	Patches	8	Back L.forearm			Y	Y			Y	Y			Y			Y		Y			Y			B.UL L.RC				BT	0	BB	N
19	Sathish	14	Male	Student	Mid	2Yrsrs	Hypo. P	Patches	5	B.thighs		Y			Y		Y	Y			Y						Y		Y			B.UL BLP				BT	0	BT	N
20	Rajendran	44	Male	Tailor	Mid	6 mon	Hypo. P Raised lesion	Patches Nodules	>20	Face B.arms Chest Back B.thighs& legs	Y				Y		Y		Y			Y	Face Ear lobe Chest		Y				Y		G & S	B.GA B.UL B.RC S.N B.LP		Ulcer R.feet	R.foot drop	LL	6+	LL	P
21	Subramanian	40	Male	Labourer	Low	3 mon	Hypo. P Numbness	Patches	>20	Neck L.arm Back chest B.legs	Y				Y		Y		Y			Y	Ear lobe		Y				Y		G & S	R.GA B.UL B.RC B.LP				LL	5+	LL	P
22	Baskar	32	Male	Labourer	Low	1Yr	Hypo. P	Patches	8	Chest L.knee L.leg		Y			Y		Y	Y			Y		Y		Y			Y			B.UL R.UL B.LP				BT	1+	BB	N
23	Devi	55	Female	House wife	Low	4Yrs	Hypo. P	Patch	1	L.arm		Y		Y			Y	Y			Y			Y			Y				B.UL L.RC				BT	0	BT	N
24	Rajesh	24	Male	Student	Mid	2 mon	Raised lesions Dry lesion	Nodules	Multiple	Chest back Abdomen B.arms B.forearms			Y		Y	Y			Y			Y			Y			Y			B.UL B.RC R.LP				LL	4+	LL	P
25	Sankar	39	Male	Security	Mid	1Yr	Raised lesion	Nodules	Multiple	Chest B.arms B.forearms Back B.thighs & legs			Y		Y	Y			Y			Y			Y			Y		G & S	R.UL R.RC R.LP				LL	5+	LL	P
26	Dilli	65	Male	Coolie	Low	8 mon	Hypo. P	maculesPatches	16	Chest Back			Y		Y		Y	Y	Y			Y		Y	Y				Y			B.UL B.RC				BB	3+	BL	N
27	Venga sabapathy	31	Male	Labourer	Low	3Yrs	Hypo. P	Patches	3	L.elbow R.arm		Y		Y			Y	Y			Y			Y					Y			R.UL R.RC				BT	0	BT	N
28	Padma	52	Female	Coolie	Low	4Yrs	Hypo. P	maculesPatches	>20	chest BackB.arms B.forearms B.legs			Y		Y		Y		Y			Y			Y			Y			B.UL B.RC R.LP		L.big toe ulcer		BL	5+	LL	P
29	Navya	7	Female	Student	Mid	1Yr	Raised lesion	Plaque	1	R.cheek		Y		Y		Y		Y		Y							Y			Y		R.UL				TT	0	TT	N
30	Surendhar	16	Male	Farmer	Low	7Yrs	Hypo. P	Patches	5	R.arm Back		Y		Y			Y	Y			Y			Y		Y			Y			R.UL R.RC				BT	0	BB	N
31	Vishnu	14	Male	Student	Mid	4 mon	Hypo. P	Patches	2	R.forearm R.leg		Y		Y			Y	Y		Y							Y			Y		R.UL R.LP				TT	0	BT	N
32	Fabuliah	19	Male	Coolie	Low	1Yr	Hypo. P	maculesPatches	>20	B.arms B.forearms chest Back B.legs			Y		Y		Y		Y			Y			Y			Y		G & S	R.GA B.UL B.RC B.LP				BL	5+	LL	P
33	Rajiv kumar nayak	28	Male	Labourer	Low	3 mon	Hypo. P	Patches	3	B.thighs		Y		Y			Y	Y			Y			Y		Y			Y			R.UL R.LP				BT	0	BT	N
34	Mariyammal	47	Male	House wife	Low	2 mon	Hypo. P swelling	Nodules edema Ulcer	Multiple	B.hands Face B.arm L.feet			Y		Y					Y						Y				Y		B.UL B.RC B.LP R.SN		L.feet ulcer		BL	5+	BL	P
35	Nagaraj	23	Male	Mechanic	Mid	3 mon	Raised lesion	Plaque	1	L.arm		Y		Y		Y		Y		Y							Y			Y		R.UL R.RC				TT	0	TT	N

36	Krishna moorthy	48	Male	Labourer	Low	1Yr	Hypo. P	macules Patches	>20	Chest Back Abdomen B.arms & forearms			Y		Y		Y				Y				Y					Y				Y			B.UL B.RC B.LP				BL	4+	BL	P
37	Vikram	13	Male	Student	Mid	8 mon	Hypo. P	Patch	1	R.cheek		Y		Y		Y		Y		Y							Y					Y			R.UL R.RC				TT	0	TT	N
38	Chandrakanthan	65	Male	No work	Low	1 mon	Raised lesion	Plaques	15	Chest Back B.arms			Y		Y	Y		Y			Y				Y					Y				Y			B.UL B.RC L.LP				BB	3+	BT	N
39	Selvam	22	Male	Labourer	Low	6 mon	Raised lesion	Nodules	Multiple	B.arms B.forearms Chest Back B.legs			Y		Y								Ear lobe Face		Y			Y			G & S	R.GA B.UL B.RC B.LP				LL	6+	LL	P
40	Jaganathan	35	Male	Coolie	Low	6 mon	Raised lesions	Plaques	10	Mid face Chest B.forearms			Y	Y		Y			Y		Y			Y		Y			Y				B.UL R.RC R.LP				BB	3+	BB	N
41	Javid	22	Male	Labourer	Low	4 mon	Hypo. P Numbness	Patches	>20	Chest Back B.arms B.forearms B.thighs	Y				Y		Y		Y			Y	Ear lobe		Y				Y		G & S	R.GA B.UL B.RC R.LP			R.claw hand	LL	5+	LL	P
42	Rama moorthy	32	Male	Farmer	Mid	1Yr	Hypo. P	Patches	3	B.arm & forearms		Y		Y			Y	Y			Y			Y			Y			Y			R.UL	Y			BT	0	BT	N
43	Lakshmi	60	Female	House wife	Low	2Yrs	Hypo. P	Patches	2	R.forearm		Y		Y			Y	Y		Y				Y		Y			Y				R.UL R.RC				BT	0	BT	N
44	Arunagiri	40	Male	Coolie	Low	6 mon	Raised lesions	Nodulels	Multiple	Face Chest Back B.arms B.forearms B.Thighs			Y						Y				Face& Ear lobe		Y			Y				B.UL B.RC R.LP B.SN			Resorption of toes	LL	6+	LL	P
45	Kavitha	18	Female	Student	Mid	8 mon	Hypo. P	Patch	1	L.forearm		Y		Y			Y	Y			Y			Y		Y				Y			B.UL				BT	0	BT	N
46	Rama chandran	39	Male	Farmer	Mid	1Yr	Hypo. P	Patches	4	Chest L.forearm		Y			Y		Y	Y			Y			Y		Y				Y			B.UL L.RC				BT	0	BT	N
47	Kannan	45	Male	Driver	Mid	2Yrs	Hypo .P	macules Patches	>20	B.arms B.forearms Chest Back B.legs			Y		Y		Y		Y			Y			Y					Y				B.GA B.UL B.RC B.LP				BL	4+	BL	N
48	Thulasi	60	Female	House wife	Low	3Yrs	Raised lesions Hypo. P	Macules Nodules	>20	Face B.arms& forearm Chest Back B.thighs	Y				Y		Y		Y			Y	Ear lobe& over macules		Y				Y		G & S	R.GA B.UL B.RC B.SN R.LP		Ulcer R.feet		LL	5+	LL	P
49	Ganesan	40	Male	Coolie	Low	9 mon	Hypo. P	Macule Patches	>20	B.arm Chest Back B.thighs & legs			Y		Y		Y					Y			Y				Y				B.UL B.RC B.LP				BL	5+	BL	P
50	Kamarasan	52	Male	Coolie	Low	3Yrs	Hypo. P Raised lesion	Macules Plaques	>20	Face Chest Back B.arms B.forearms B.Thighs	Y				Y		Y		Y			Y	Face& Ear lobe		Y					Y	G & S	B.GA B.UL B.RC L.SN B.LP			Resorption of toes	LL	6+	LL	P

Tuberculoid Leprosy

Borderline Tuberculoid

Mid borderline Leprosy

Borderline Lepromatous Leprosy

Lepromatous Leprosy

Lepromatous Leprosy – Earlobe Infiltration

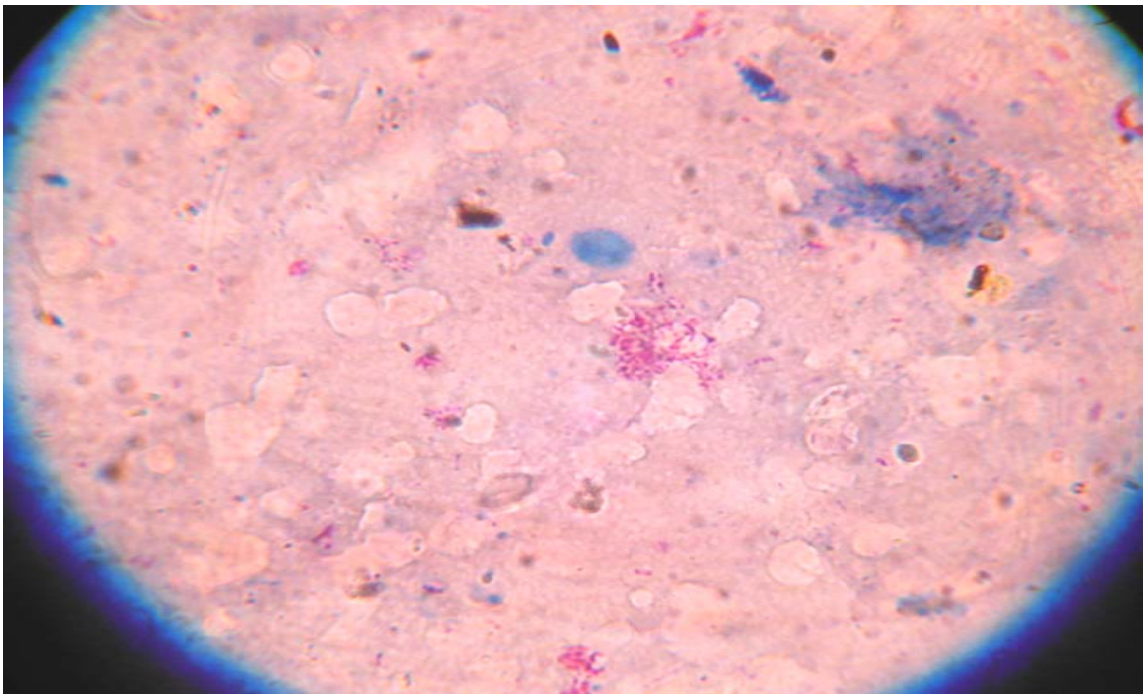
LL – Leonine facies

LL – Icthyotic Patch

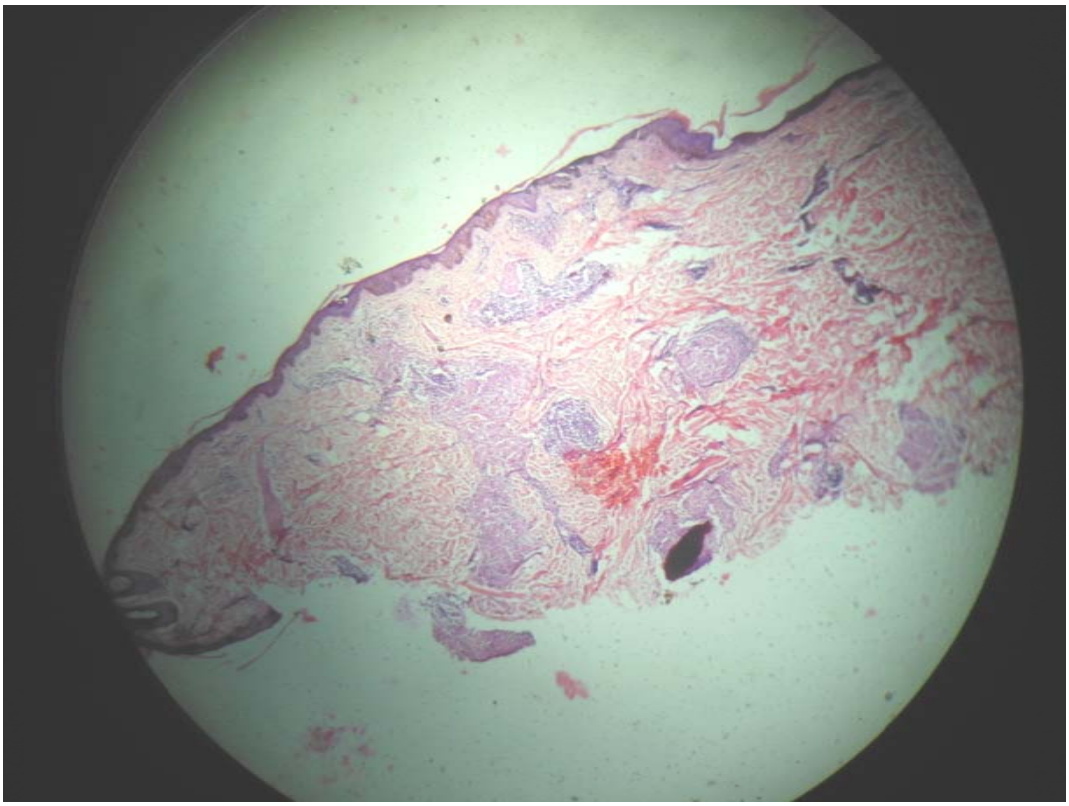
Greater Auricular Nerve Enlargement

Histoid Leprosy

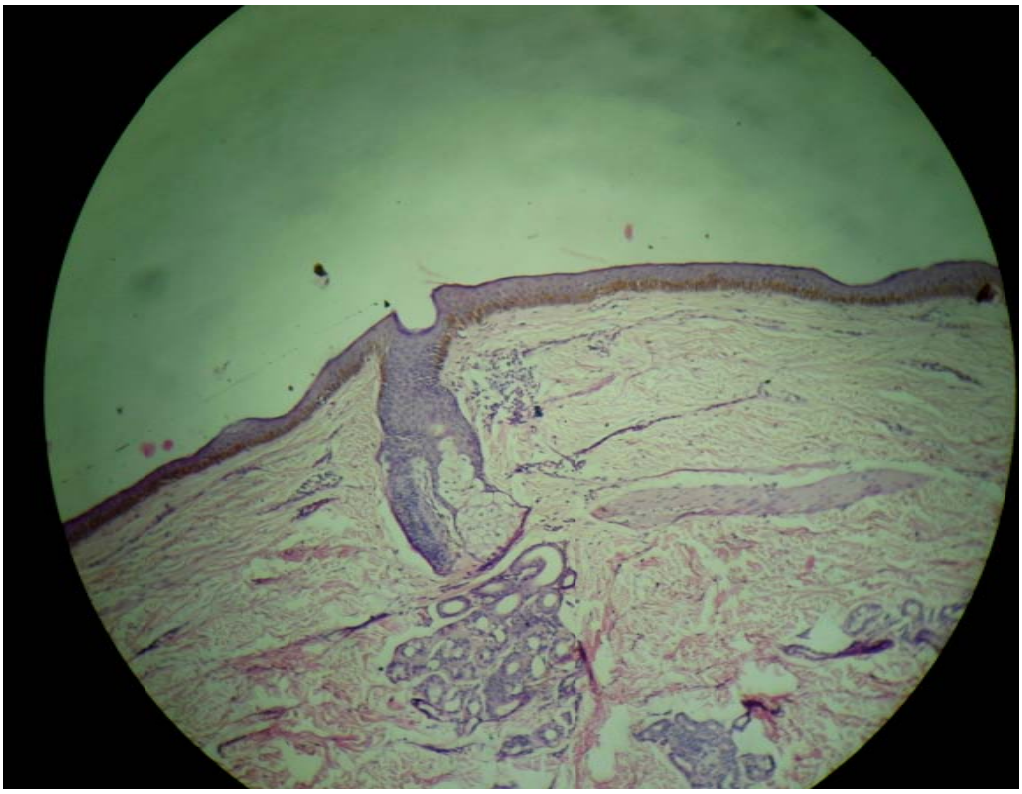
Slit Skin Smear - AFB



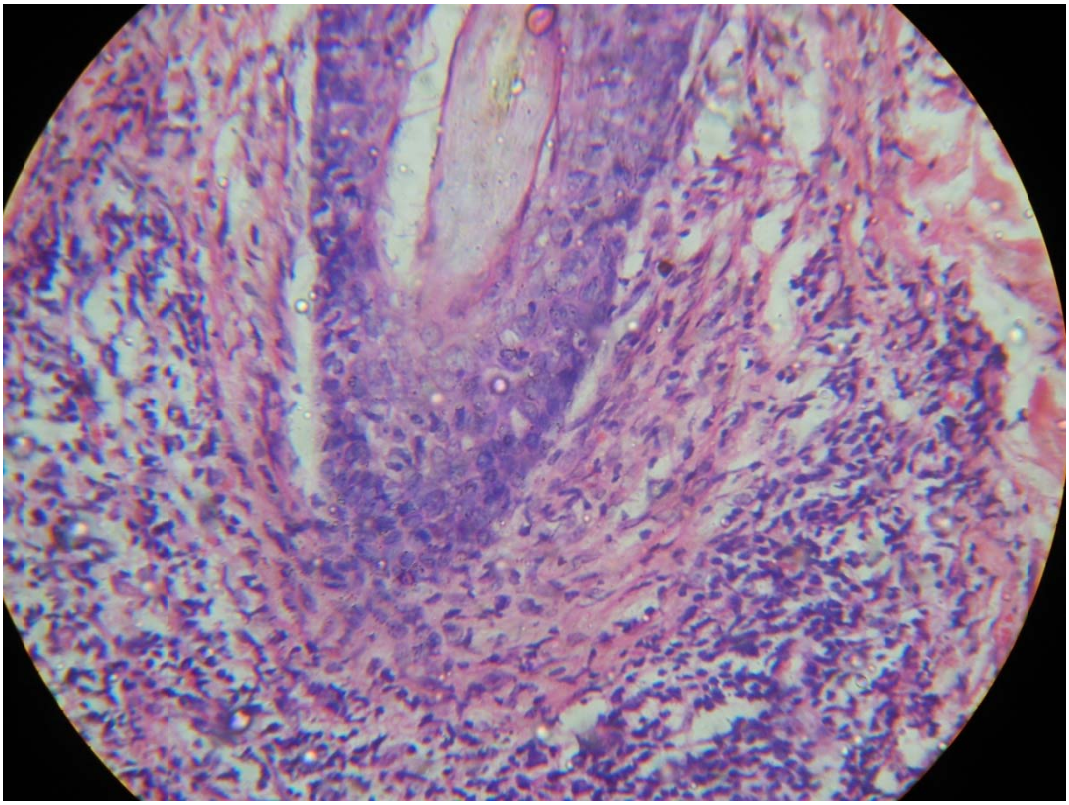
Tuberculoid Leprosy



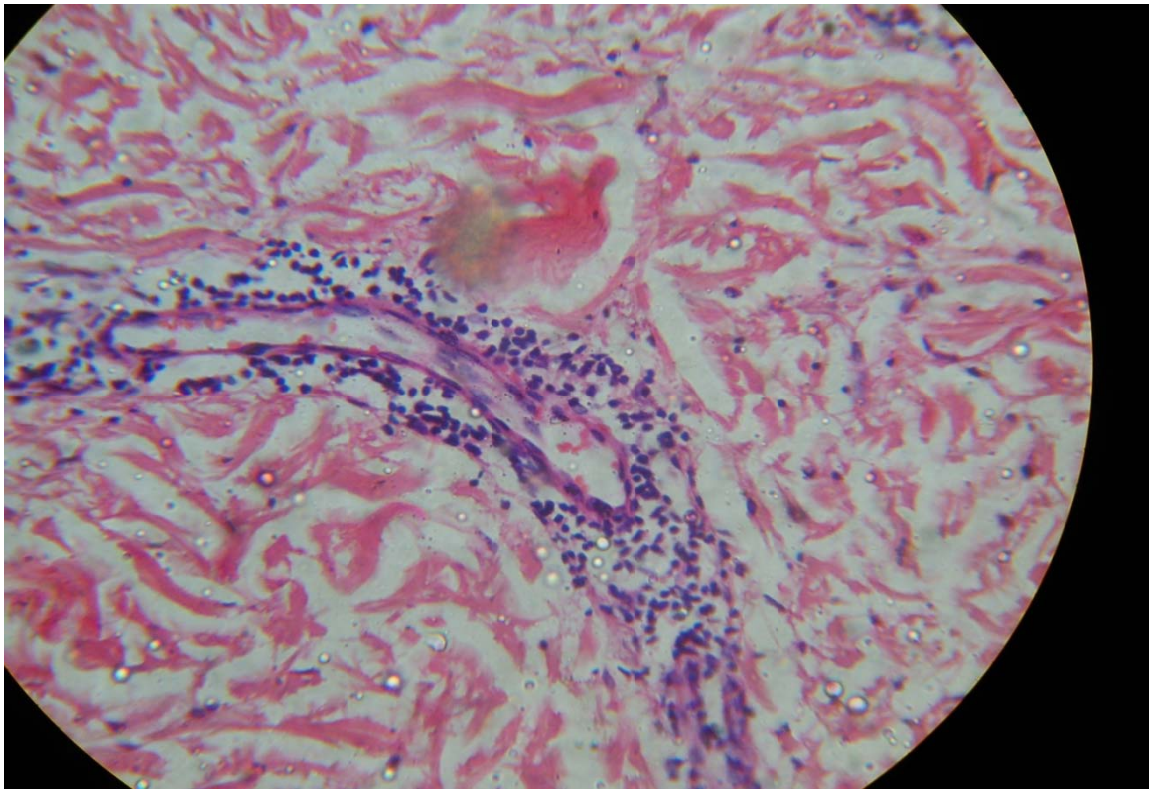
Borderline Tuberculoid



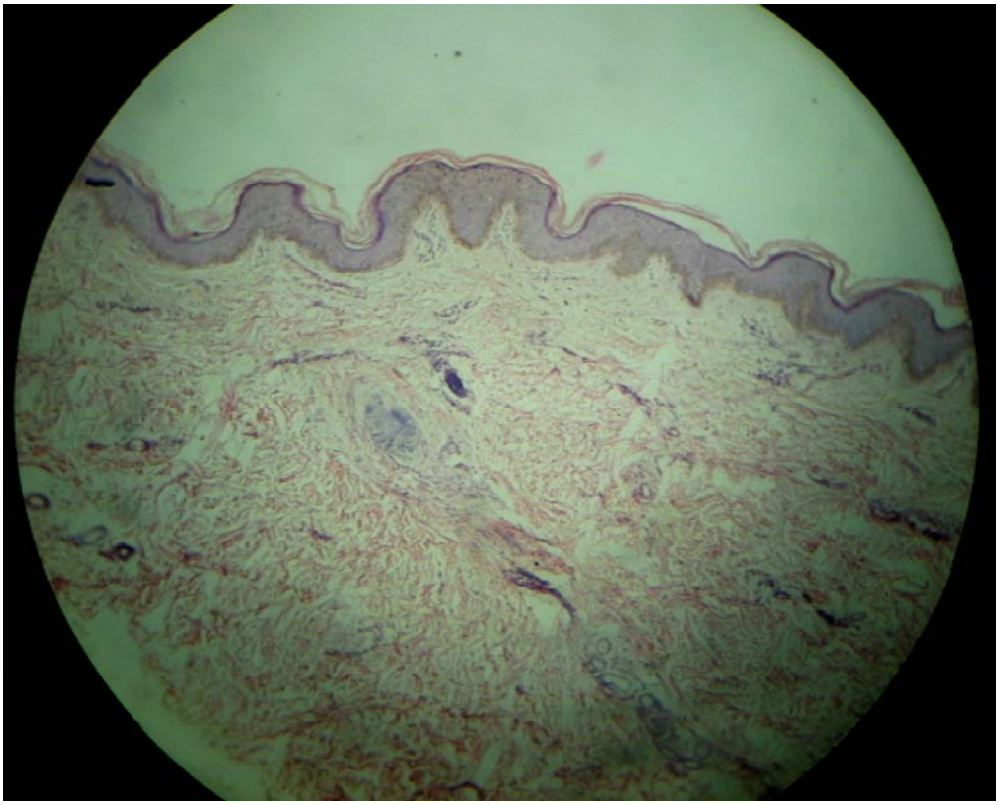
BT – Perifolicular infiltration



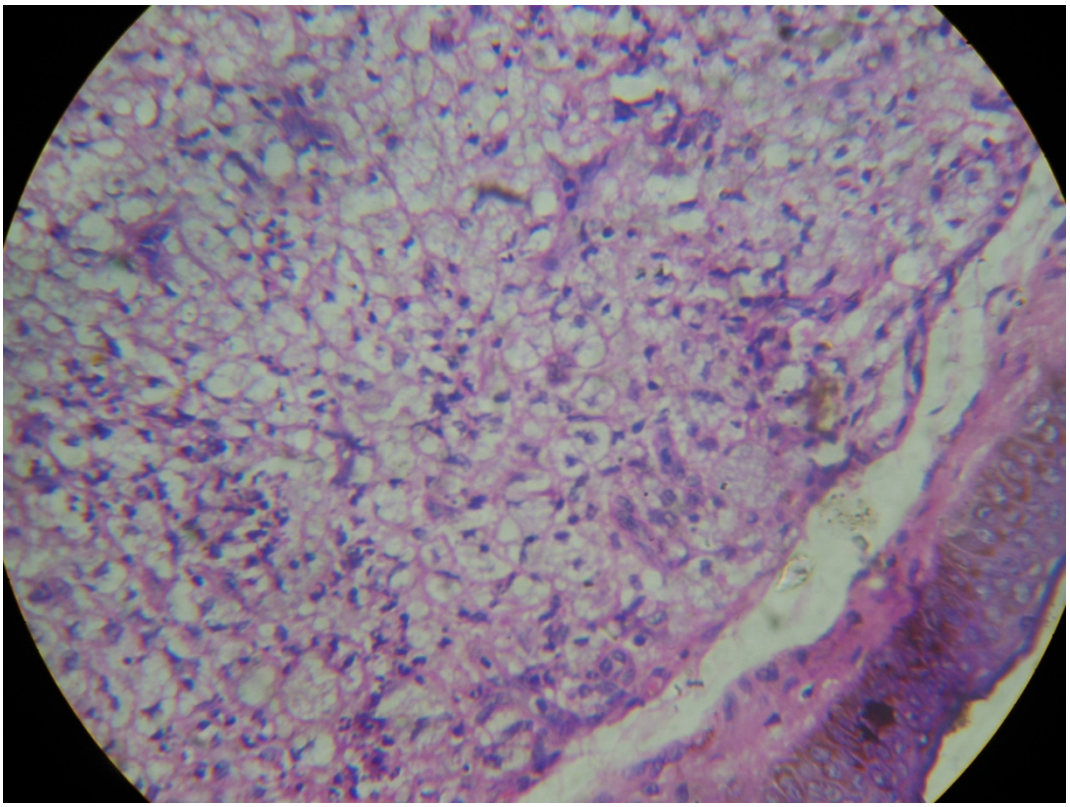
BT – Perivasulcar Infiltration



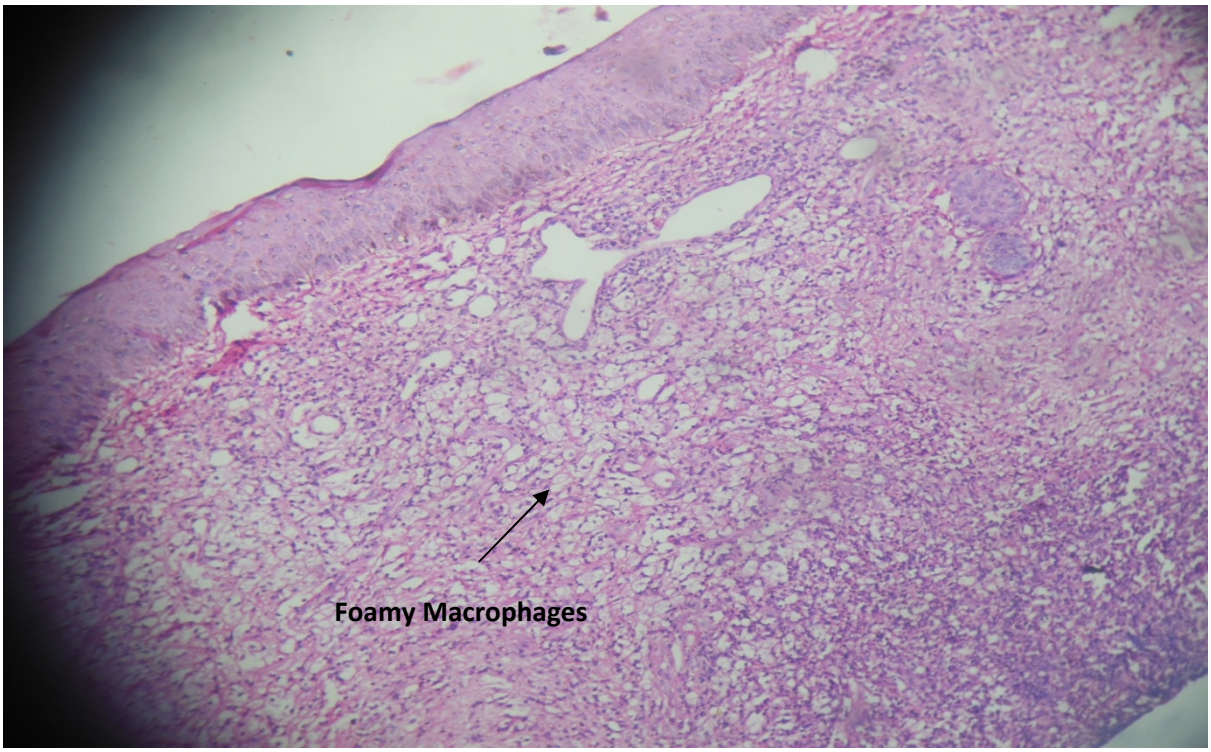
Mid Borderline Leprosy



Borderline lepromatous leprosy



Lepromatous Leprosy



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